CHIASMA®

Chiasma Overview

January 2020

NASDAQ: CHMA

Forward-Looking Statements

These slides and the accompanying presentation contain forward-looking statements and information. The use of words such as “may,” “might,” “will,” “should,” “expect,” “plan,” “anticipate,” “believe,” “estimate,” “project,” “intend,” “future,” “potential,” or “continue,” and other similar expressions are intended to identify forward-looking statements. These statements include, without limitation, those statements regarding the development and potential commercialization of octreotide capsules, conditionally named MYCAPSSA, for the treatment of acromegaly, the potential development of octreotide capsules for other indications and utilization of the TPE platform for other therapies, the data from the CHIASMA OPTIMAL trial and whether the data and the rest of the regulatory submission will support the approval by the FDA of Chiasma’s resubmission of its new drug application, or NDA, for octreotide capsules, statements regarding the timing of NDA regulatory review, including the completion of the review by the PDUFA goal date, and potential approval, statements concerning the nature of the FDA’s review of any such NDA submission and whether the data submission will be sufficient to support regulatory approval, statements concerning the timing of potential commercial launch of MYCAPSSA in the United States and the release of topline date from the MPOWERED phase 3 trial, statements concerning the commercial or therapeutic potential of MYCAPSSA, if approved, and statements concerning future indication and pipeline expansion plans, and statements concerning the market potential of MYCAPSSA. All forward-looking statements are based on estimates and assumptions by Chiasma’s management that, although Chiasma believes them to be reasonable, are inherently uncertain. All forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially from those that Chiasma expects. For example, there can be no guarantee that the FDA will agree that the NDA resubmission supports marketing approval or that MYCAPSSA qualifies for marketing approval in the United States based on the results from the CHIASMA OPTIMAL trial and other information contained in the NDA. Further, as Chiasma has disclosed, in order to have product availability of MYCAPSSA for a potential commercial launch in the fourth quarter of 2020, following anticipated approval of the NDA, Chiasma expects to submit two manufacturing supplements to its NDA for an additional active pharmaceutical ingredient, or API, manufacturer and for an additional commercial-scale manufacturing site of the API manufacturer currently referenced in the NDA, the review of which will require FDA review and approval of the manufacturing process, facility, equipment and procedures in place at each manufacturer in accordance with the FDA’s current good manufacturing practice requirements and may require additional regulatory inspections of each manufacturer, which could prevent or delay approval of any such supplement to the NDA and prevent or delay commercial launch. In addition, even if Chiasma is able to obtain approval of the additional API manufacturer or additional API manufacturing site, there can be no guarantee that Chiasma will be able to secure API or commercial octreotide capsules in sufficient quantities, in a timely manner or at all and initiate the planned commercial launch of octreotide capsules. These and other potential risks, uncertainties and other important factors are described under the heading “Risk Factors” in our Form 10-K for the year ended December 31, 2018 filed with the Securities and Exchange Commission, or SEC, as well as in Chiasma’s subsequent filings with the SEC. Undue reliance should not be placed on any forward-looking statement, which speak only as of the date on which it was made. Chiasma undertakes no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events or otherwise, except as required by law.

Unless otherwise noted, all references to acromegaly market sizes are Chiasma internal estimates. This presentation is intended only for communications with investors. MYCAPSSA is an investigational drug that has not been approved by the FDA or any other regulatory agency. The safety and efficacy of this drug candidate has not been established by any agency.

Chiasma: On A Mission to Improve Patients' Lives

CHIASMA®

- Biopharmaceutical company with a lead asset in registration with the FDA
- Focused on patients who face challenges with their existing treatments
- Management team and board with significant experience

Mycapssa® (octreotide) capsules

- If approved, the first oral SSA therapy in an injectable-only market
- Potential addressable market in acromegaly of ~$800M globally*
- NDA resubmitted and accepted for review; PDUFA date June 26, 2020 with a planned Q4:2020 commercial launch
- Mycapssa has the potential to become the new standard of pharmacologic care
- Patent protection through early 2036 in U.S. (pending in EU)

TPE® TRANSIENT PERMEABILITY ENHANCER

- Validated technology platform that enables oral delivery of select peptides
- Potentially attractive opportunities in select therapeutic areas with no oral therapies

Financial Position

- ~$92M in cash, cash equivalents and marketable securities as of December 31, 2019

* Company estimate

2020 – A Potentially Transformational Year

Timing	Anticipated Key Milestones	Status
Q1:2020	Mycapssa Octreotide Capsule NDA Acceptance from the FDA	✓
Q1:2020	Mycapssa OPTIMAL Phase 3 Data Presentation at ENDO	
Mid-2020	Publish CHIASMA OPTIMAL Phase 3 data in Peer Reviewed Journal	
Mid-2020	Mycapssa PDUFA Decision	
Q4:2020	Mycapssa API Manufacturing Supplements Decision/Commercial Supply Availability	
Q4:2020	Mycapssa U.S. Launch	
Q4:2020	MPOWERED Phase 3 Top-Line Data	
2020	Expand Pipeline Utilizing TPE Technology	

Commercial Launch Anticipated Q4:2020

Acromegaly U.S. Market Summary

- A rare and debilitating hormonal disorder caused by a benign pituitary tumor treated by surgery and pharmacologic therapy; prevalence estimated to be approximately 75 per million

- Somatostatin analog (SSA) injections are broadly used as first line pharmacologic treatment
  - ~8,000 Acromegaly patients in the U.S. are on SSAs
  - Prior trials with injectable octreotide LAR[1] showed 42-57% maintenance IGF-1 response rate
  - ~90% of patients treated within ~1,000 accounts

- Injections carry significant treatment burdens for patients (i.e., pain, injection site reactions, sub-optimal symptom control, loss of independence, etc.)
  - Treatment burdens are increasingly being recognized by physicians

- The 2018 global market for SSAs in the treatment of acromegaly is estimated at ~$800 million with U.S. estimated at ~$400 million

- Price for SSAs range from $55,000 / year of treatment (Sandostatin) to $165,000 (Signifor)

- If approved, Mycapssa positioned to potentially become the first oral SSA

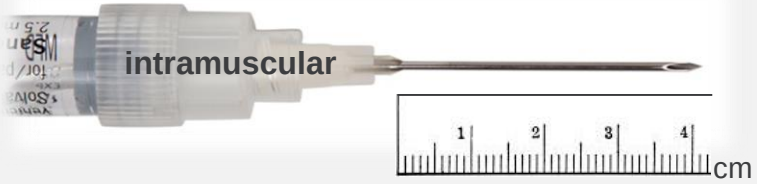
Acromegaly represents an attractive commercial opportunity for Chiasma

CHIASMA®

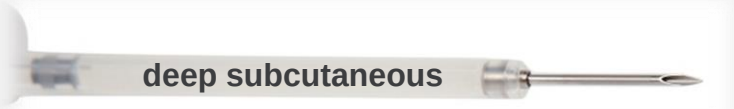
1. Sandostatin LAR prescribing information 2019

Current Injection Therapies Carry Significant Treatment Burdens[1]

Novartis' Octreotide LAR: 19 or 20 Gauge



Ipsen's Lanreotide Depot: 18 or 19 Gauge



Reference: Insulin Needle: 30 Gauge

Pain	• 70% experienced pain during injection; half of these experienced continuing pain days later
Injection Site Reactions	• Hardness (48%), nodules (38%), swelling (28%), bruising (16%) and inflammation (7%)
Suboptimal Symptom Control	• 52% report symptoms worsen toward the end of the monthly dosing interval • 32% controlled patients still complain about symptoms
Emotional Impact	• 36% feel loss of independence due to chronic injections
Lost Work Days	• 16% regularly miss work for injections (averages 11 days / year)

Compelling need for an oral therapeutic option

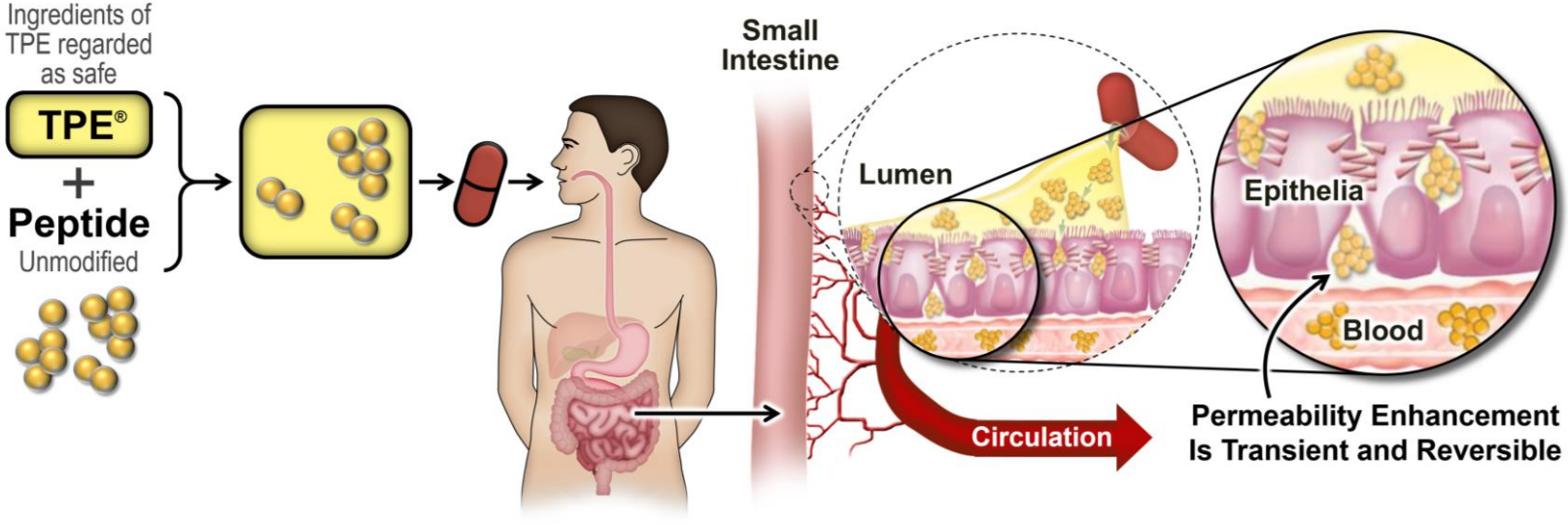
CHIASMA

1. Strasburger et al. Patient reported outcomes of parenteral somatostatin analogue injections in 195 patients with acromegaly. *Eur J Endocrinol*. 2016 Mar;174(3):355-62

TPE® Delivery Platform

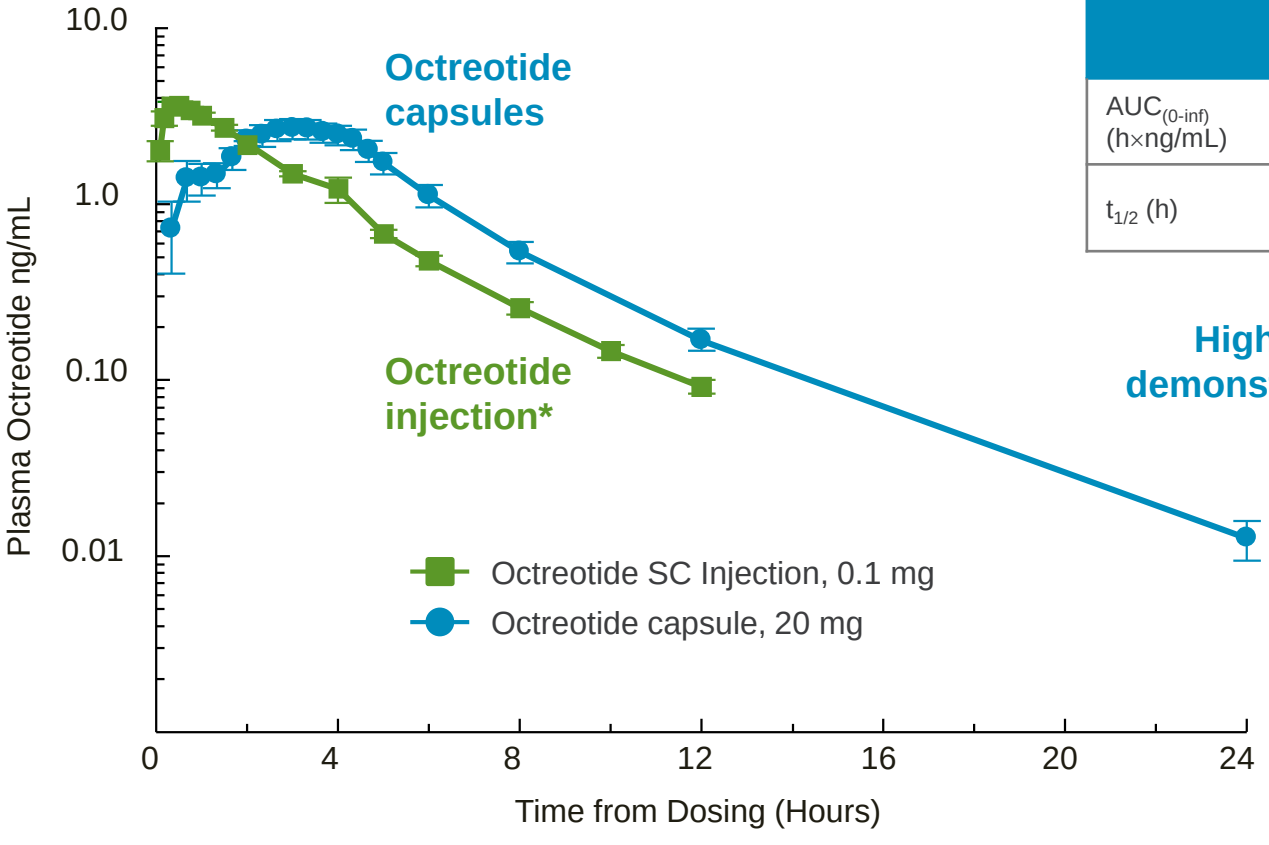
Peptide is protected by TPE® from degradation…

…then absorbed intact at therapeutic levels.



TPE enhances oral bioavailability, potentially allowing for oral formulations of injectable-only therapies

Plasma Levels of Octreotide Comparable to SC Injection



	Octreotide SC (n=14)	Octreotide Capsule (n=24)
$AUC_{(0\text{-}inf)}$ (h×ng/mL)	13.7 (2.29)	17.0 (9.66)
$t_{1/2}$ (h)	2.27 (0.25)	2.66 (0.73)

Data are Mean (SD)

Higher AUC from oral octreotide demonstrates longer residence time

Data are mean ± SEM.
* Octreotide subcutaneous (SC) injection = Sandostatin®, IR injection, Novartis.

Mycapssa – Robust Clinical Database

Cynomolgus Monkeys	• Toxicology studies for 1, 3, and 9 months
	  − No adverse macroscopic or microscopic changes were detected in GI or liver
	  − No signs of inflammation

Phase 1 Trials	• 9 trials, **172** healthy subjects:
	  − No documented serious adverse events
	  − Abdominal discomfort was most commonly reported AE (~15%; octreotide related)

Phase 3 Trials	• Phase 3 studies (CH-ACM-01, 302 MPOWERED, and 303 OPTIMAL); **151 + 146 + 28** patients with acromegaly treated with Mycapssa:
	  − Adverse events were consistent with the known safety profile of octreotide and disease burden of acromegaly
	  − No injection-related AEs
	  − No formulation-related AEs
	  ▪ No signal for increased risk of GI infections
	  ▪ No signal for increased inflammatory markers (WBC, CRP)
	  ▪ No antibodies detected

Mycapssa Pivotal Trial Clinical Summary

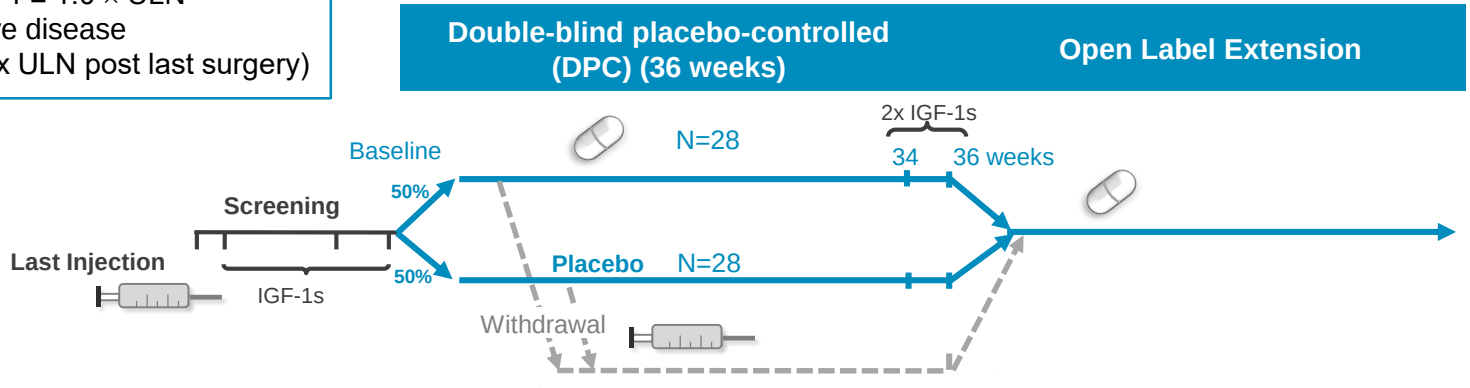
- TPE enhances oral bioavailability potentially allowing for oral formulations of injectable-only peptide therapies
- CHIASMA OPTIMAL phase 3 trial under a SPA agreement **met its primary endpoint and all secondary endpoints**
  - NDA resubmitted to the FDA December 26, 2019
  - Notified of the FDA's acceptance on January 10, 2020
  - FDA granted PDUFA date of June 26, 2020
- CHIASMA MPOWERED phase 3 trial (E.U.) top-line data expected to be released in Q4 2020

Focused U.S. commercial readiness planning underway

OPTIMAL Phase 3: Multinational, Randomized, Placebo-Controlled Study

Octreotide Capsules Versus Placebo Treatment In MultinationAL Centers

Eligibility Criteria:
- Average IGF-1 ≤ 1.0 × ULN
- Confirm active disease (IGF-1 ≥ 1.3 x ULN post last surgery)



Primary Endpoint
- Proportion of patients who maintain biochemical response (average of week 34 and 36 IGF-1 ≤ 1.0 x ULN)

Pre-defined Withdrawal Criteria (Both Arms)
- IGF-1 ≥1.3 x ULN for 2 consecutive visits on the highest dose and exacerbation of clinical signs / symptoms
- Early terminated patients followed up to 36 weeks on injections, per protocol

Subject Disposition and Demographics
- 56 patients, 28 per group (octreotide capsules or placebo)
- 38% from the US
- All patients completed trial
  - ✓ No missing primary endpoint data
- Baseline characteristics well balanced between the groups

Key Clinical Information from CHIASMA OPTIMAL Trial

- The mean IGF-1 of the octreotide capsules group (n = 28) at the end of treatment was maintained within the normal range (0.97 x ULN) while it was 1.69 x ULN in the placebo group
- 75% of patients on octreotide capsules achieved an IGF-1 <= 1.1xULN at end of treatment
- 75% of patients in the octreotide capsules group (n = 28) successfully completed the trial on oral therapy (i.e., did not rescue to prior injectable treatment)
- 90% of all patients who completed the trial in active arm elected to continue on octreotide capsules

OPTIMAL Phase 3: Primary and All Secondary Endpoints Met

Endpoints	Octreotide (N=28)	Placebo (N=28)	P-value
Primary			
Proportion Maintaining IGF-1 Response	58%	19%	0.008
Secondary			
Proportion Maintaining GH Response	78%	30%	0.001
Time to IGF-1 >1.0 × ULN	Median > 36 weeks	Median = 16 weeks	< 0.001
Time to IGF-1 ≥1.3 × ULN	Median > 36 weeks	Median = 16 weeks	< 0.001
Rescued to Prior Injectable	25%	68%	0.003

All enrolled patients completed the study

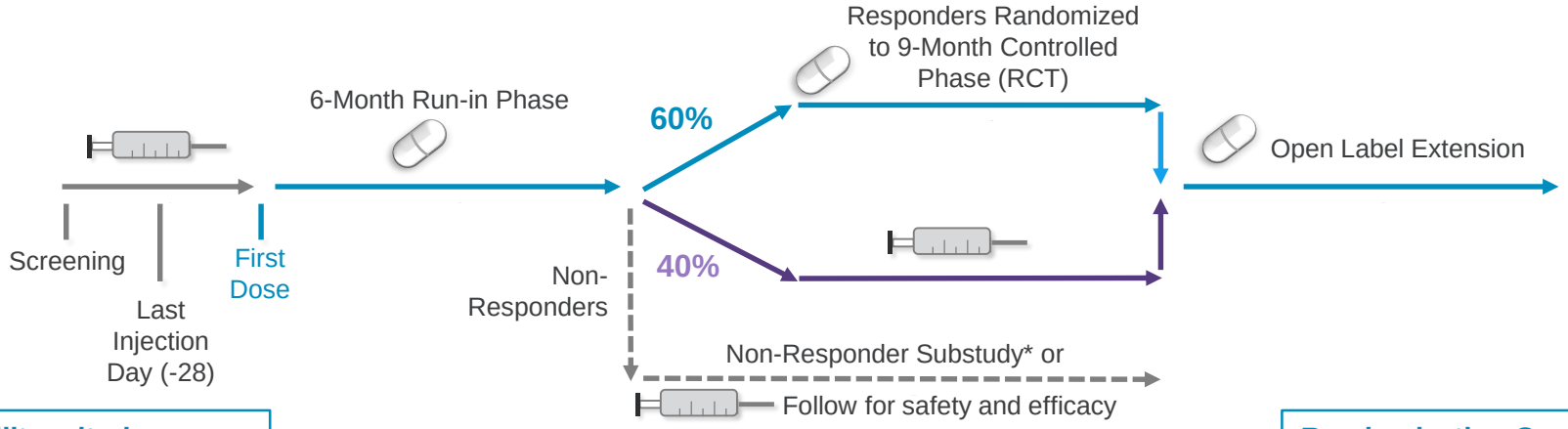
Octreotide Capsules Appeared Safe and Well Tolerated

Subjects with:	Octreotide Capsules n	Octreotide Capsules %	Placebo n	Placebo %
At least one TEAE	28	100.0	27	96.4
Treatment-Related TEAE	18	64.3	15	53.6
SAEs	2	7.1	1	3.6
Treatment-Related SAEs	0	0.0	0	0.0
Severe TEAEs	3	10.7	7	25.0
TEAE Leading to Study Drug Discontinuation	2	7.1	1	3.6
TEAEs of Special Interest (acromegaly symptoms)	15	53.6	26	92.9

TEAE - Treatment-Emergent Adverse Events; SAEs – Serious Adverse Events; TEAEs of special interest: e.g. headache, perspiration, joint pain, fatigue, soft tissue swelling

MPOWERED: Multinational, Randomized, Non-inferiority Study

Maintenance of Acromegaly Patients with Octreotide Capsules Compared With Injections – Evaluation of REsponse Durability



Eligibility criteria:

- IGF-1 <1.3 x ULN and GH<2.5 ng/mL

Randomization Completed:

- 63% responder rate per protocol a/o January 2020

Primary Endpoint:

- The proportion of patients who are biochemically controlled throughout the RCT phase. A patient will be considered biochemically controlled if their IGF-1 Time Weighted Average (TWA), during the RCT phase is < 1.3 × ULN.

Key Secondary Endpoints:

- Proportion of patients who maintain or reduce the overall number of active acromegaly symptoms at the end of RCT
- Acromegaly Treatment Satisfaction Questionnaire (ACRO-TSQ) at the end of the RCT phase

CHIASMA

*Non-responders at selected centers will be offered the opportunity to determine if they can respond to a combination of oral octreotide and the drug cabergoline.

A Differentiated Rare Disease Commercial Launch Strategy

Traditional Rare Disease Launch Challenges

- ***Patients can be hard to identify –*** investments needed for patient identification
- ***Doctors are critical stakeholders and may be unfamiliar with MOA or a NCE –*** investment and time needed for education
- ***Patients need to be educated on benefits –*** investment and time needed to build patient advocacy
- ***Payers need to find budget to pay for new orphan therapies*** – Mycapssa is for the most part a replacement of existing therapy, if approved

MYCAPSSA Expected Launch Advantages

- ***Minimal investment needed for MOA or disease awareness***, which allows for education to focus on the treatment burdens
- ***Physicians prefer SSA analogs*** *as their standard of treatment choice*
- ***Nurses and patients are key*** to switching behavior
- ***Significant room to improve patient experience -*** Competitors' execution and pull-back in the market leaves gaps and creates dissatisfaction amongst patients and providers
- ***Robust data package*** from Chiasma OPTIMAL demonstrating patients maintain biochemical response on Mycapssa

Expected Key Drivers For A Successful Launch

Patients[1,2,3,4,5]

- 90% of patients on oral octreotide who completed the OPTIMAL trial continued into the Open Label Extension
- Patients experience symptoms, often later in the injection cycle, that is increasingly being recognized by HCPs
- Strong precedents for oral preference to injectables from relevant analogues

KOLs

- Clinical programs involved many KOLs
- Strong familiarity with Chiasma and Mycapssa
- Ongoing planned initiatives on education

Community Endos / HCPs[6]

- Endos open and willing to inform patients of Mycapssa:
  - ~57% will inform all of their patients
  - ~39% will inform appropriate candidates
- Increasing acceptance of treatment burden

Patient Advocacy

- Strong relations with an active advocacy community that is well-established
- Ongoing planned engagements and sponsorships

MACRO Registry – Management of Acromegaly

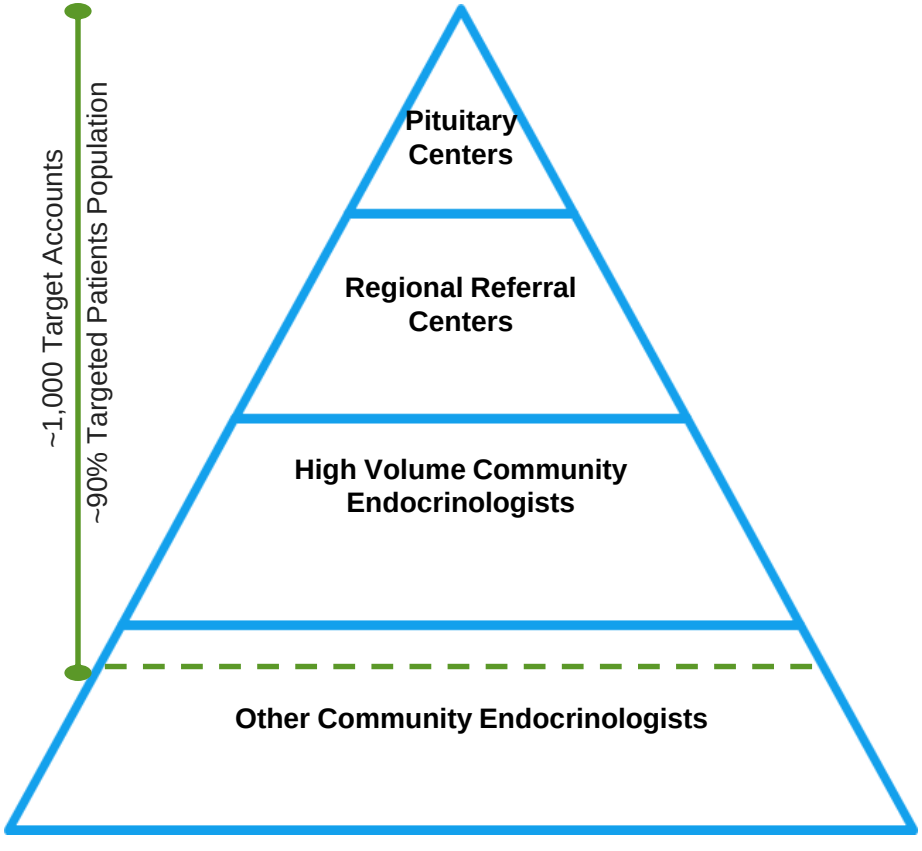
- Scheduled to begin U.S. enrollment in early 2020 at > 40 sites for the first Disease State registry in acromegaly
- Goal is to collect real-world data on treatment burden and effectiveness of various treatments

[1] Melmed S et al. *J Clin Endocrinol Metab.* 2015 Apr;100(4):1699-708. [2] Strasburger C et al. ENDO 2015 Poster PP09-4. [3] Patient Reported Outcome Data from Acromegaly Patients Treated with Injectable Somatostatin Analogues in Routine Clinical Practice. Presented at ENDO, Abstract #5468. March 23-26, 2019. [4] Relationship between Responses from Acromegaly Patients Treated with a Stable Dose of Injectable Somatostatin Analogues in Routine Clinical Practice and their Endocrinology Health Care Professional regarding treatment Outcomes. Presented at ENDO Abstract #5468, March 23-26, 2019. [5] Biochemically Controlled Acromegaly Patients on a Stable Dose of Injectable SSAs in Routine Clinical Practice Still Remain Symptomatic. Presented at ENDO, Abstract #8138, March 23-26, 2019. [6] U.S. Endocrinologists Self-Reported Current and Future Somatostatin Analog Prescribing Behaviors for the Medical Management of Acromegaly, Market Modelers. N=102 endocrinologists, Sept. 2015. .

CHIASMA®

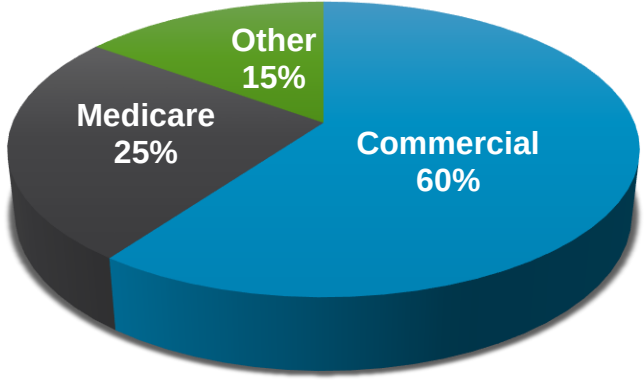
Orphan, Addressable U.S. Acromegaly Market Opportunity

Addressing the Acromegaly Market [1]



Product	Route	July 2019 WAC $/Yr.[2]	Covered by Major Payers[3]
Sandostatin® (octreotide LAR)	IM	$55,000	Yes
Somatuline® (lanreotide Depot)	Deep SC	$88,000	Yes
Somavert® (pegvisomant)	SC	$158,000	Varies by plan
Signifor® (pasireotide LAR)	IM	$165,000	Yes

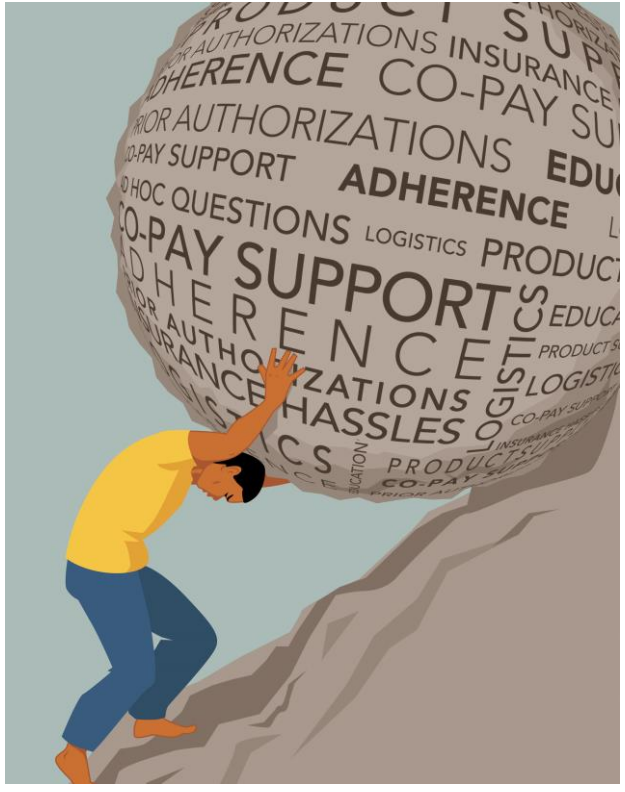
Estimated Payer Mix [1]



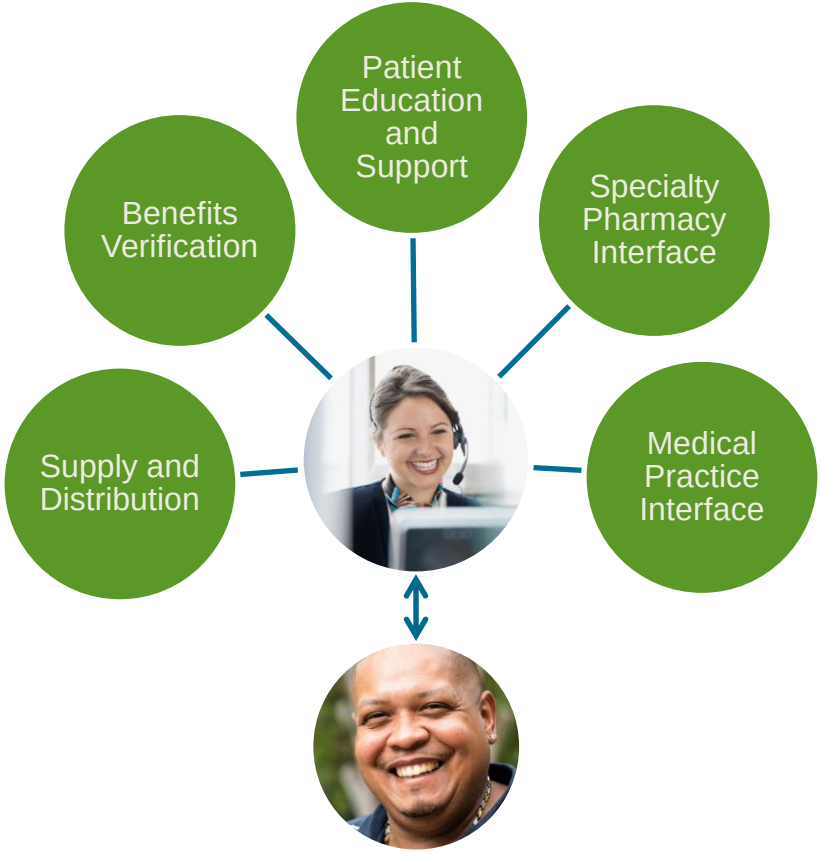
[1] Company estimates. [2] Weighted average cost for mid-range doses annually as provided by Red Book Online (July 10, 2019) rounded to nearest $1k. [3] Tag & Associates, Inc. Dec 2018. Based on published medical and drug coverage policies of United Healthcare, Anthem, Aetna/Humana and Cigna.

Patients Are Our Focus

Patients are Carrying the Burden Today

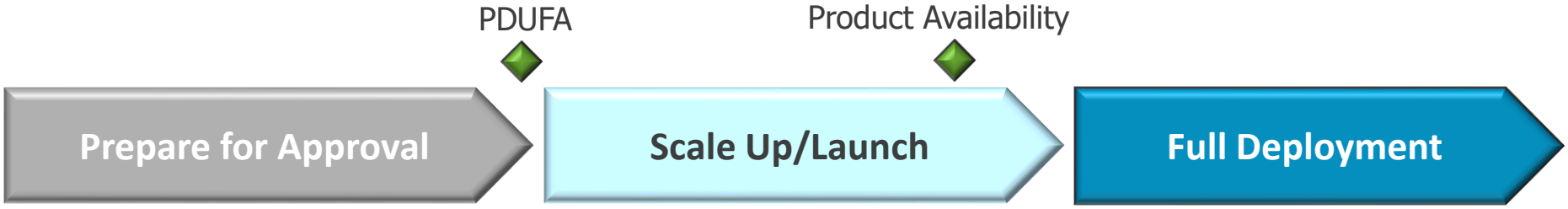


Chiasma Case Managers Will Help Alleviate the Load



CHIASMA®

Planned 2020 Approval and Launch Activities



- Profile clinicians and patient flows
- Engage physicians, nurses, payers and patients on disease and treatment burden awareness
- Develop resources to facilitate switch
- Build supply chain

- Engage high-value accounts
- Ensure successful early starts
- Create referral networks
- Build full-scale launch organization

- Call on targeted accounts
- Build broad prescribing base
- Leverage referral networks

Planning 30 to 50 Customer Facing Positions

Key Leaders Appointed

RAJ KANNAN
Chief Executive Officer
- Over 25 years of industry experience from field sales, brand and payer marketing, managing country business units, to leading global business franchises
- Led multiple successful product launches both in the US and globally
- Solid breadth and depth of commercialization experience in chronic, specialty, and rare diseases across multiple therapeutic areas

SCOTT MCCONNELL
VP Medical Affairs
- Previously Senior Director of Medical Affairs at Chiasma in 2015 & 2016; rejoined 2019
- Former Medical Affairs roles at Kaledio Biosciences, Alkermes, and Cubist Pharmaceuticals / Merck & Co.
- Pharm.D. from Creighton University School of Pharmacy and Allied Health Professions; Clinical Residency at Basset Healthcare; Post-Doctoral Fellowship at The University of Arkansas for Medical Sciences

DEREK BROWN
VP Marketing
- Former Marketing roles at Alexion, which included leading the global team responsible for the commercialization of Ultomiris® in two ultra-rare hematology diseases (PNH and aHUS), and Boehringer Ingelheim
- Independent consulting experience with clinical-stage biopharmaceutical companies in rare and ultra-rare disease
- M.B.A. from The Tuck School of Business at Dartmouth; B.A. in Cellular Structure and Function and in Economics from Middlebury College

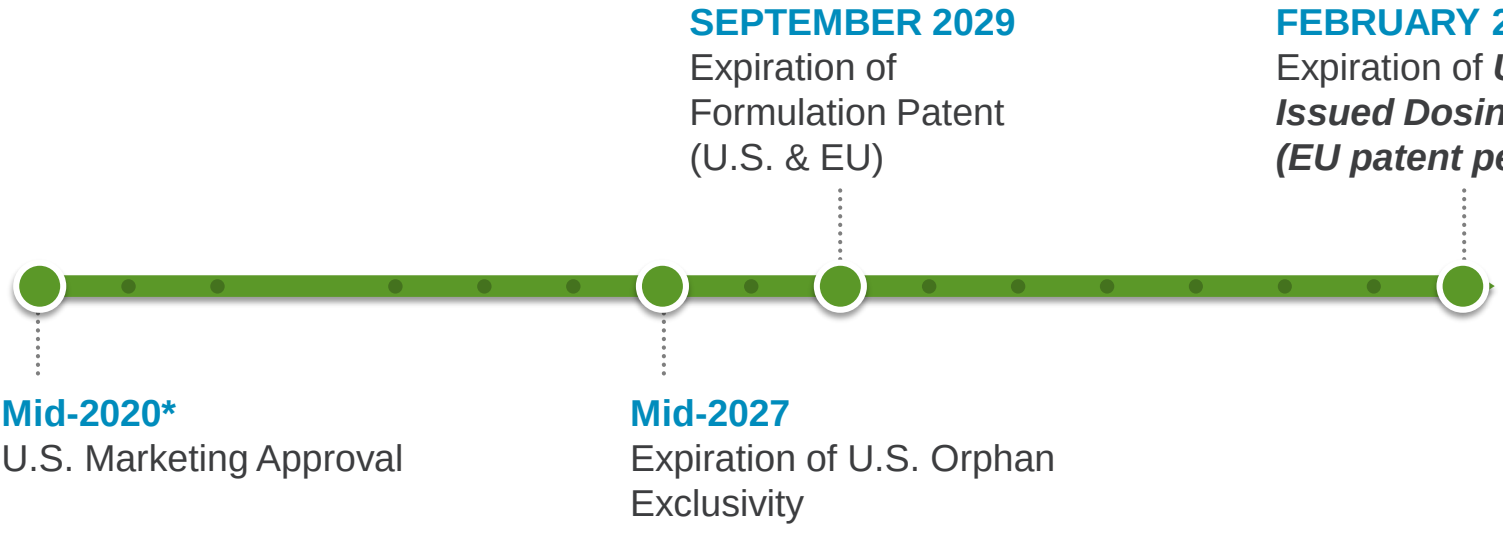
DAN THORNTON
VP Market Access and Patient Services
- Previously VP of Market Access and Patient Services at Chiasma in 2015 & 2016; rejoined 2019
- Former Market Access roles at Flexion Therapeutics, Shire, Targanta Therapeutics, Therion Biologics, Biogen Idec, and Johnson & Johnson
- M.B.A. from The Wharton School; B.A. in Health Policy from Duke University

ANAND VARADAN
Commercial Strategic Advisor
- Previously Chief Commercial Officer at Chiasma in 2015 & 2016
- Built commercial organization and successfully launched orphan oncology drug for Karyopharm Therapeutics as CCO (2018 to 2019)
- General Management at Amgen in US and internationally across numerous therapeutic areas (1999-2015)
- M.B.A. from The Simon Business School at the University of Rochester; B.A. in Zoology from George Washington University

CHIASMA®

Mycapssa® Estimated Exclusivity Timeline*

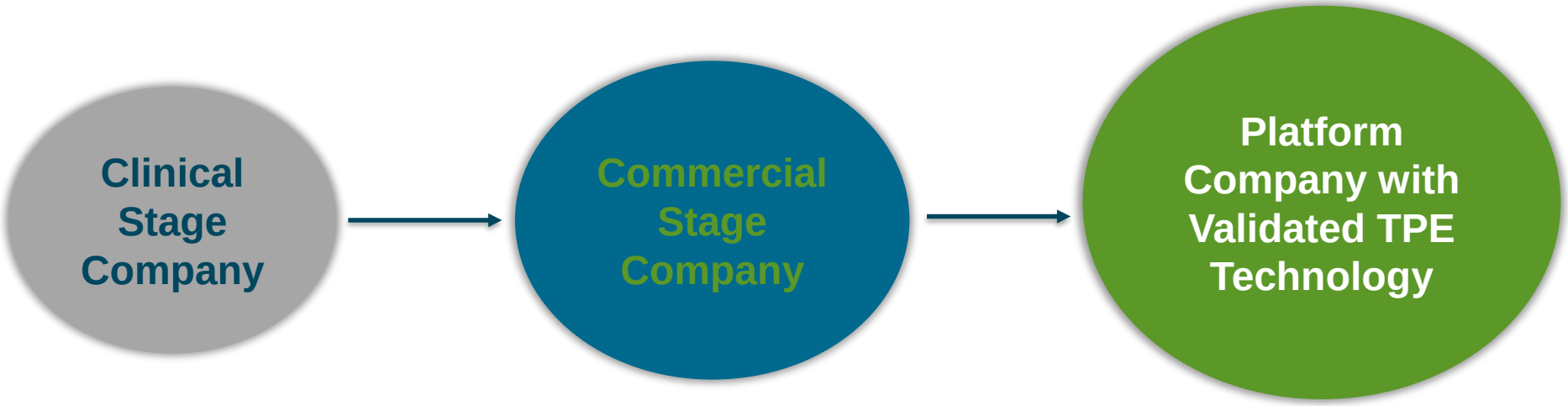
Strong patent and exclusivity position



NOTES: Generics may enter the market at the end of the patent exclusivity and our patents may be challenged at any time; If a generic challenger wins a patent challenge, the generic can enter the market after expiration of regulatory and orphan exclusivity.

* For illustration purposes only: Timeline assumes mid-2020 PDUFA approval.

2020 – A Potentially Transformational Year



Well positioned for potential launch of first commercial product in 2020

CHIASMA®

Thank you

January 2020

NASDAQ: CHMA