



Hyloris and Purna Female Healthcare

A New Partnership in Women's Health

5 February 2021



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Today's Presenters



Prof. dr. Gilbert Donders
Gynaecologist, Professor
Antwerp University Hospital



Bart Peeters
CEO Purna Female
Healthcare



Stijn Van Rompay
CEO Hyloris
Pharmaceuticals

A Unique Partnership

To add value to women's health by developing an innovative therapy to treat severe and recurrent vulvovaginal candidiasis (rVVC) with a patented, proprietary topical combination product of Miconazole (MCZ) and Domiphen Bromide (DB)

Purna Female
Healthcare (PFH)

- Belgian based spin-off (Purna Pharmaceuticals and Creafund)
- Completed early-stage R&D activities with University of Antwerp and KU Leuven, including all pre-clinical work and responsible for further product development, clinical trials, manufacturing, regulatory affairs, IP
- IP and know how in-licensed from University of Antwerp and KU Leuven

Hyloris

- Committed to milestone related investments of up to €4.27M, of which €1.27M at signing, and to support PFH
- Owns 20% of PFH, eligible to receive up to a maximum of 45% of the net profits generated by PFH
- Responsible for out-licensing and commercialisation

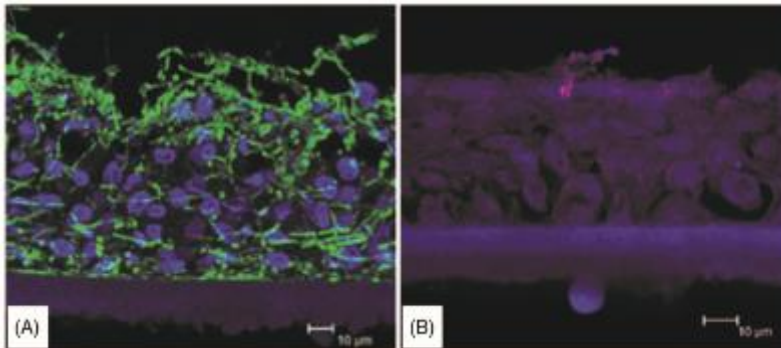
Vulvovaginal Candidiasis



Vulvovaginal Candidiasis – Pathogenesis

- Infection caused by *Candida* sp. yeast
- Causes irritation, vaginal discharge and intense itchiness of the vagina and the vulva
- **Affecting 1 in every 2 women during their life**

Uncomplicated VVC (80%)	Complicated VVC (20%)
Sporadic or infrequent VVC AND Mild-to-moderate VVC AND Likely to be <i>C. albicans</i> AND Non-immunocompromised women	Recurrent VVC (4 or more episodes / year) OR Severe VVC OR Non- <i>albicans</i> candidiasis OR Women with diabetes, immunocompromising conditions (e.g. HIV infection), debilitation, or immunosuppressive therapy (e.g. corticosteroids)



Reconstituted human vaginal epithelium infected with *C. albicans* (A) and *C. glabrata* (B) ⁽²⁾

Vulvovaginal Candidiasis – SoC & Unmet Needs

Standard of Care (SoC)	
LOCAL	SYSTEMIC
	



Challenges
<ul style="list-style-type: none">• Azole resistance• Liver toxicity• Drug-Drug interactions• Pregnancy and miscarriage warnings• Lack-of-efficiency in complicated VVC



There is a high unmet medical need for improved treatment options

Severe and rVVC – Debilitating, Chronic Conditions

- **Approximately 20% of all VVC patients**
- **No effective treatments available due to drug-resistant biofilm formation in yeast**
- **Patients associate severe and rVVC with **oppression, isolation, embarrassment, frustration, powerlessness, sadness, and hopelessness to the point of despair****
- **\$14.4 Bn annual estimated economic burden from lost productivity**



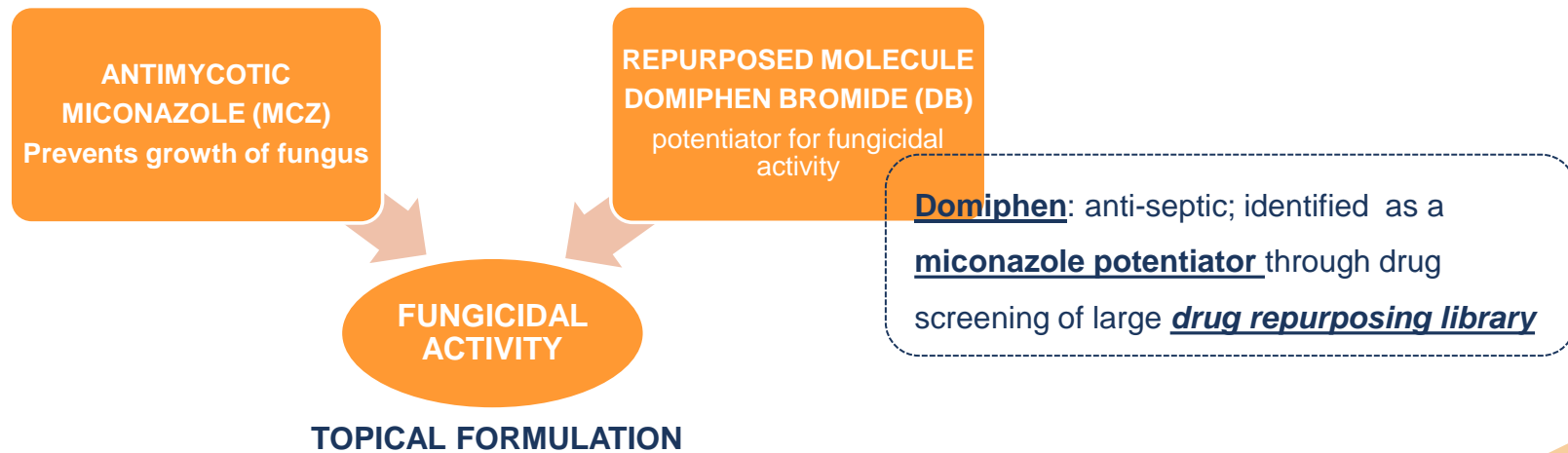
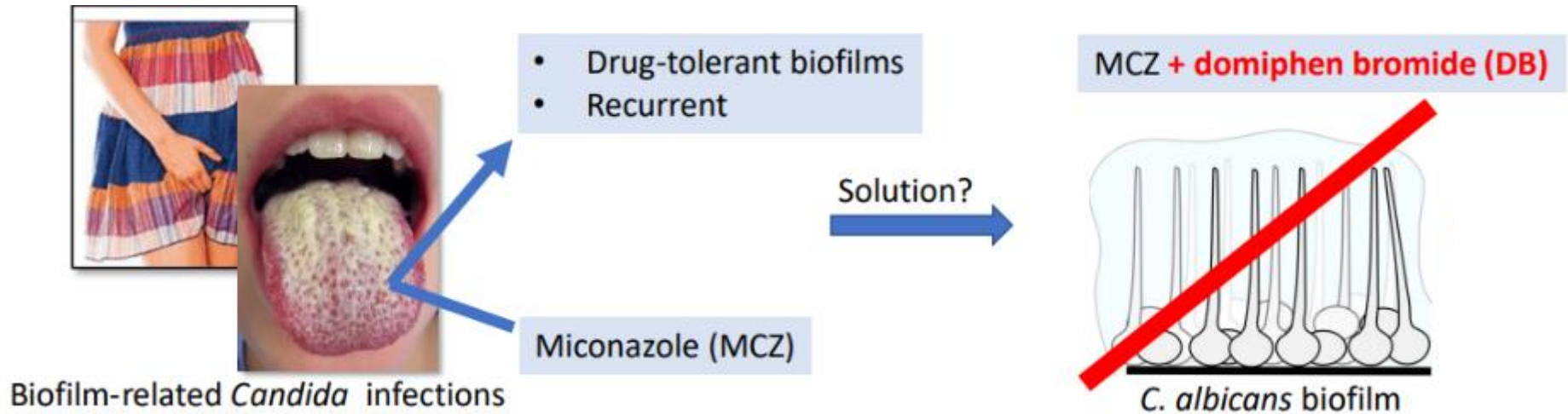
Mindset is defined by pain and suffering

We heard a perspective bullied by negative forces, loss of control, shame, isolation and fear

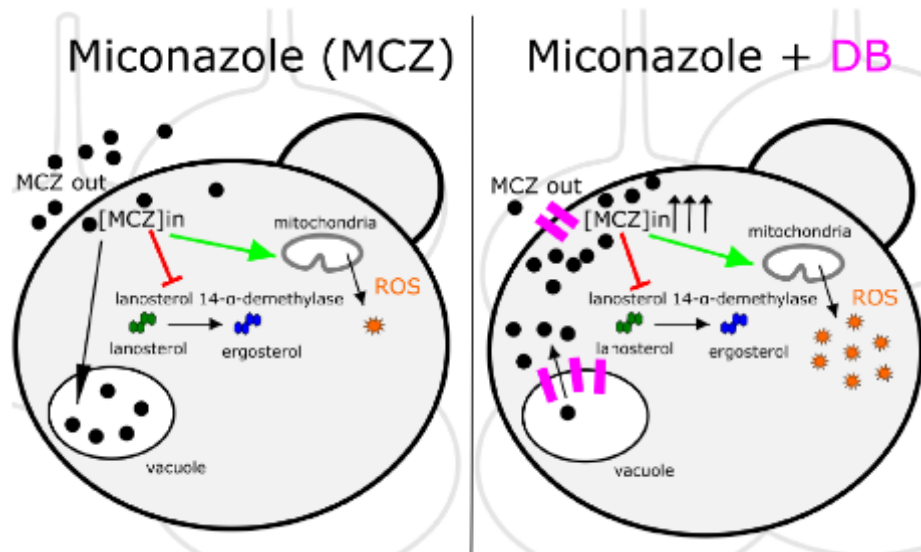
Potential Solution



Potential Solution – Novel MCZ-DB Combination



Novel MCZ-DB Mode of Action – *In Vitro* Validation



Domiphen Bromide:

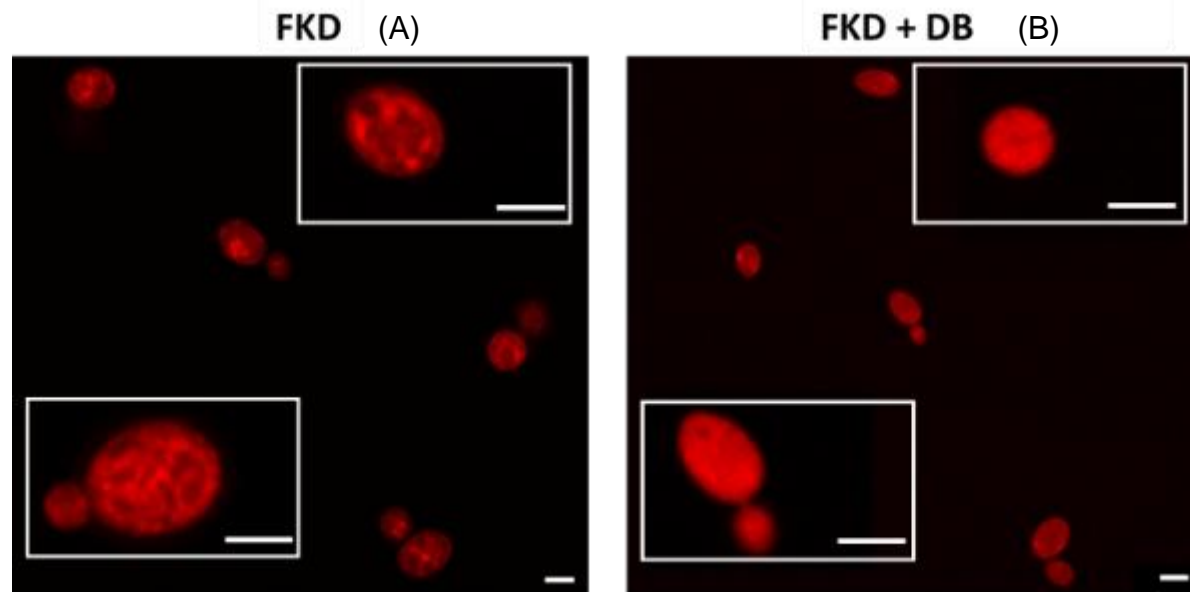
- Enables increased FKD (azole) uptake in *Candida* cells at low doses
- Alters cytoplasmatic distribution of high FKD doses
- Negatively affects vacuolar integrity, thereby releasing vacuole-sequestered MCZ

Increased intracellular MCZ availability results in

- increased ROS* generation
- fungicidal antibiofilm activity

Sources: Benhamou R. I., Bibi M., Steinbuch K. B., Engel H., Levin M., Roichman Y., Berman J. and Fridman M. (2017). Real-Time Imaging of the Azole Class of Antifungal Drugs in Live *Candida* Cells. *ACS Chemical Biology*, 2017; 12, 1769–1777; KU Leuven

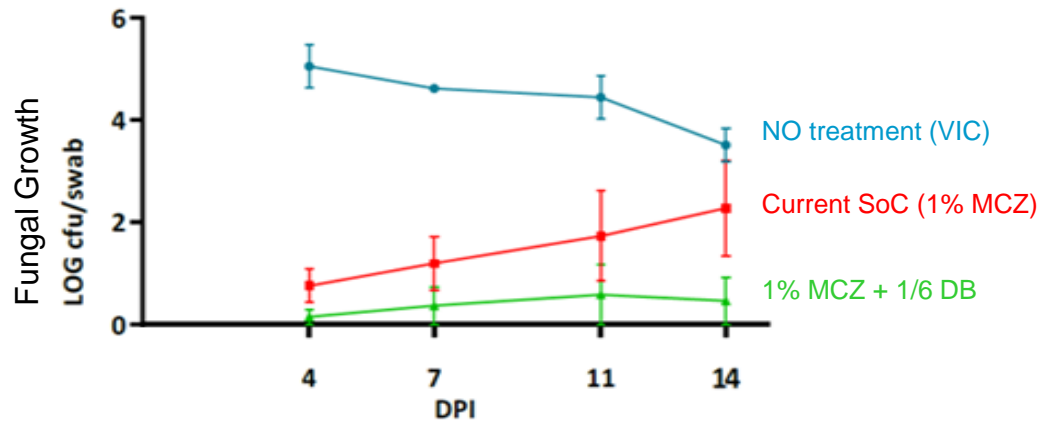
Novel MCZ-DB Combination – *In Vitro* Mode of Action



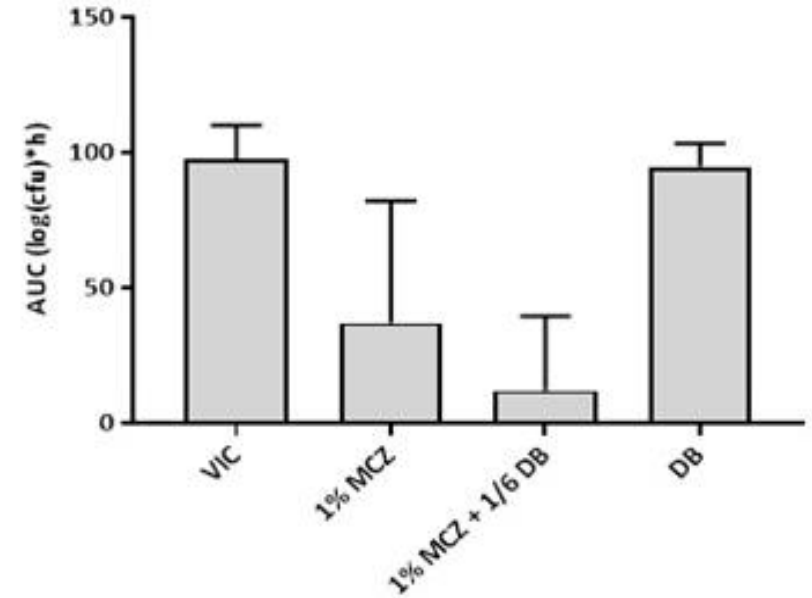
Effect of domiphen bromide (DB) on cytoplasmic distribution of fluorescently labeled ketoconazole derivative (FKD) in *C. glabrata* BG2 planktonic stationary phase cultures

High Fluorescence panel B shows high-uptake of the combo drug

Novel MCZ-DB Combination – Highly Effective *In Vivo*



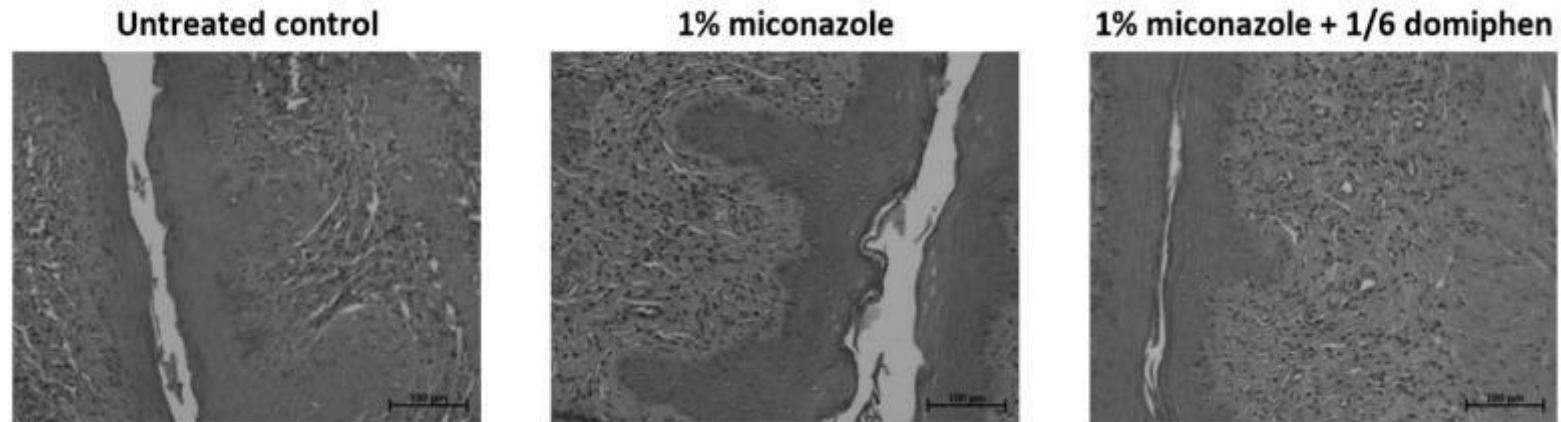
Intravaginal fungal burden in log colony forming units (cfu) per swab during different therapies expressed in days post-infection (DPI)



Degree of infection expressed in area under the curve (AUC) after 4 days of treatment and 10 days of follow-up in function of different formulations

Domiphen Bromide (DB) significantly enhances miconazole efficacy *in vivo*

Novel MCZ-DB Combination – *In Vivo* Tolerance



Vaginal tissue after hematoxyline-eosine staining of untreated control, 1% miconazole and 1% miconazole + 1/6 domiphen bromide. Different groups showed adequate cornification (dark grey zone), meaning they are all-in oestrus (due to effective hormone treatment)

MCZ-DB combination treatment does not enhance systemic absorption of one or both active compounds

No apparent lesions could be observed

MCZ-DB – IP position

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
24 January 2019 (24.01.2019)

WIPO | PCT

(10) International Publication Number
WO 2019/015975 A1

(51) International Patent Classification:
A61K 31/4174 (2006.01) *A61K 9/107* (2006.01)
A61K 45/06 (2006.01) *A61K 47/44* (2017.01)
A61K 47/34 (2017.01) *A61K 31/34* (2006.01)
A61K 9/06 (2006.01) *A61K 47/18* (2017.01)

(21) International Application Number:
PCT/EP2018/068192

(22) International Filing Date:
05 July 2018 (05.07.2018)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
1711512.2 14 July 2017 (18.07.2017) GB
LU100445 20 September 2017 (20.09.2017) LU

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(81) Designated States (unless otherwise indicated for every kind of national protection available): AE, AG, AL, AM, AU, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.13:
— of inventorship (Rule 4.13(ii))

(54) Title: COMPOSITIONS AGAINST CANDIDA INFECTIONS

International Publication Number (IPN):

WO 2019/015975 A1

Patent Number:

GB1711512

Main Claim:

A composition for topical use comprising miconazole or a salt thereof and domiphen bromide as active ingredients for use in treating or preventing infection with *Candida* spp.

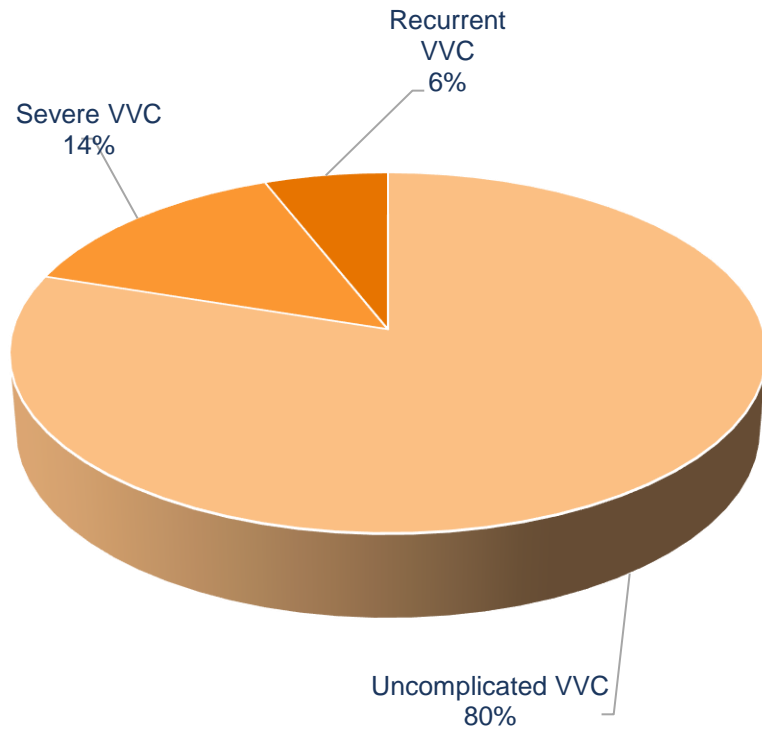
July 2018: IPO

January 2020: “National entry” in EU & US

Large Opportunity



Global VVC – Market Dynamics











Total number of drug products sold	± 175.000.000
Average annual growth rate	5.5%
Classification	Creams: 47% Pessaries: 34% Other: 19%

No innovation over the past few decades

Opportunity to disrupt the market with novel MOA MCZ-DB combination therapy

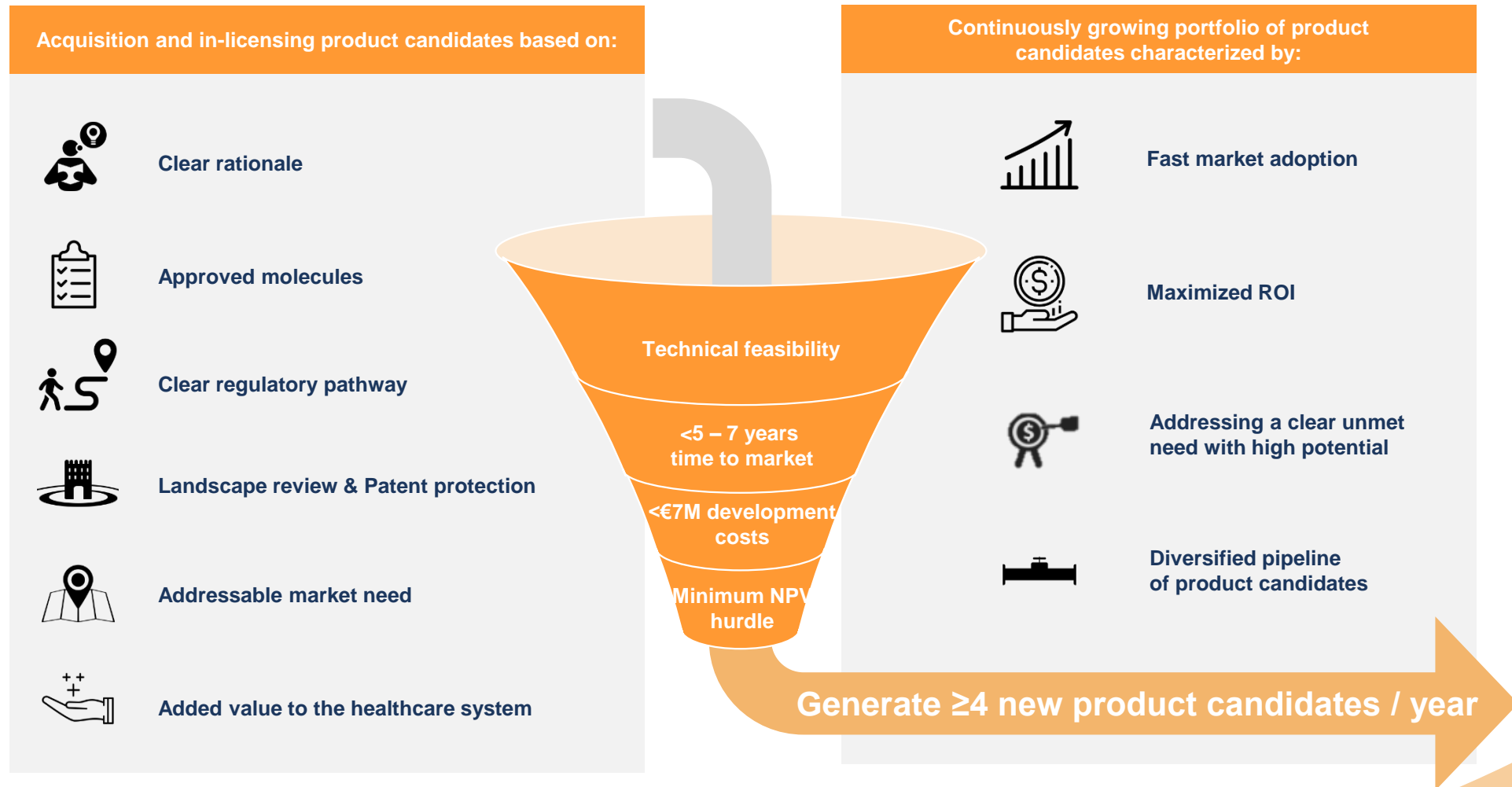
Recurrent Vulvovaginal Candidiasis (rVVC)

- Characterized by ≥ 3 episodes of acute vulvovaginal candidiasis per year
- Affects 6-9% of women during child-bearing years, 138 million women annually globally, 372 million women over their lifetime - estimated to increase to almost 158 million women annually by 2030
- Causes discomfort, pain and emotional distress, all of which can be severe and can have a profound impact on women suffering from this condition

		Female population	Females aged 15-54 y	Base case burden	Prevalence per 100,000 females
World		3,430,235,000	1,968,068,000	137,627,000	3,871
USA		158,718,000	86,125,000	5,992,000	3,775
Japan		65,317,800	30,894,000	2,193,000	3,357
Germany		42,342,000	21,977,000	1,532,000	3,619
France		32,656,000	16,573,000	1,157,000	3,543
UK		31,544,000	16,708,000	1,169,000	3,707
Italy		31,149,000	16,066,000	1,137,000	3,650
Spain		23,381,000	12,891,000	926,000	3,961

→ Global annual prevalence of severe vulvovaginal candidiasis (14% of total VVC) estimated to be > 2 times higher than the global annual prevalence of recurring vulvovaginal candidiasis (6% of all VVC)

PFH Partnership – Perfectly Fits within Hyloris' Strategy



Novel MCZ-DB Topical Treatment – Key Takeaways

- Opportunity to address unmet medical need in severe and recurrent vulvovaginal candidiasis
- Potential first innovation since decades
- Novel MOA, potential first-in-class to address biofilm formation and drug-resistant *Candida* infections
- Developed for local topical application
- Strong *in vitro* and *in vivo* results
- Strong IP position

Next steps: start Phase 2 dose-finding study later in 2021

Q&A

