!" #&/
4;O <548G=>3> 70AB>AC20==O ;V:0@AL:>3> 70A>1C

"

(CLOTRIMAZOLUM)

!:;04:
4VNG0 @5G>28=0: :;>B@8<07>;;
1 B01;5B:0 B@8<07>;;C 100 <3;
4>?>28=8: ;0:B>70, <>=>3V4@0@0; :@>E<0;L :0@B>?;O=89, :8A;>B0 048?V=>20, =0B@VN
3V4@@>:0@1>=0B, <03=VN AB50@0B, :@0=5<VN 4V>:A84 :>:;>W4=89 1572>4=89, =0B@VN
;0C@8;AC;LD0B.

V:0@AL:0 D>@<0. "01;5B:0 203V=0;L=V.
A=>2=V DV78:>-EVABV: 1V;V B01;5B8, 42>>?C:;V, 7 >1@V7=8<8 :@0O<8, ?@>4>230AB>W D>@@@<8,
70>:@C3;5=V 7 >4==3> 1>:C B0 7 BC?8< :@0T< 7 V=H>3>.

$0@<0:>B5@0?52B8G=0 3@C?0. @>B81@V B0 0=B8A5?B8G=V 70A>18, I> 70AB>A>2CNBLAO 2
3V=5:>;>3>VW. ;>B@8<07>;;. >4 "% G01A F02.

$0@<0:>;>3VG=V 2;0AB82>ABV.
$0@<0:>48=0<V:0
;>B@8<07>;; T ?>EV4=8< V;C 7 H8@@>:8< A?5:B@>< W ?@>B813@81>2W 4VW =0 1V;LHVABL
?0B>35==8E 3@81V2. 5E0=V7< 4VW :;>B@8<07>;;C ?>;O30T 2 :;>C20==V A8=B57C =C;;5W>>28E
:8A;>B B0 ?@>B81@5W=V2, 0 B0:>6 A8=B57C 5@3>AB5@0;;;C C 3@@>1V;>28E :;VB8=0E ::VB8W=0E, I> <0T =0;V4:>>><
?>H>465==O WE ::VB8W==>W >1>;>=:8 B0 703815;V ::VB8W=.
;>B@8<07>;; 4VT 3>;>2=8< G8=>< =0 45@<0>B2VB8;V, 4@>V646>?>4V1=V B0 ?;VA=OV2V 3@81818, 48
<>@@@D=V 3@81818.
@8 2V4?>2V4=8E C>20E B5@0=8?52B8G=0 :>=C5=B@0@VO :;>B@8<07>;;C V3@0T F8E?V2 3@81V2
AB@0>=>2;OB @?@81;87=> <5H5 =V6 0,062 8,0 /<;; AC1AB@0B0.
5E0=V7< 4VW :;>B@8<07>;;C ?>2O7V=8W 7 ?5@58H=>N DC=3VAB0B8G=>N 01> DC=3VF84=>N
0:B82=VAB, 70;56> 2V4 :>=F5=B@0@VW :;>B@8<07>;;C C
In vitro :;>B@8<07>;; >1<565 5;5<5=B0@:V B, I> ?@>;VD5@@CNBL; A?@>4V 3@81V2 <0NBL ;8H5
=57=0G=C GCB;82VABL.
>40B:>2> 4> 0=B8<V:>B8G=>W 4VW :;>B@8<07>;;; B0:>6 4VT =0 3@0<-?>78B82=V <V:@>>@30=V7<8
(AB@5?B>B@V:>:8, AB0DV;>:>:8, *Gardnerellavaginalis)* B0 3@0<-=530B82=V <V:@>>@30=V7<8 *(Bacteroids)*.
In vitro :;>B@8<07>;; ?@8385VGV @>7<=>65==O *Corynebacteria* B0 3@0<?>78B82=8E :>:V2 (70 28=OB:>< *Enterococci)* C :>=F5=B@0@VW 0,5-10
$0@<0:>:V=5B8:0.
@8 ?V52>3?2>@0;L==>W 20V=V=:0@:V 3-10 % 2V4 7030;L=>W :V;L:>ABV :;>B@8<07>;; 2A;>:V:0TBLAO. VA;O 2A>
<>VAL:C20==O :;>B@8<07>;; ?5@5B2>@NBLAO =0 =50:B82=V <5B01>;VB8-E;>@D5=V;-4-
3V4@@>:A8D5=V;-D5=V;<5B0=. @81;87=> 50 % 2V4 9>3> 7030;L=>W :V;L:>ABV :;>B@8<07>;; 7 D5:0;VW=8<8
=0:>?8G5==O< 8H5 1 % ?@5?0@0B0 :V;L:>ABV :@>1;5=V :5@V

;V=VG=V E0@0:B5@8AB8:8.
>:070==O.
=D5:FVW C 4V;O=FV AB0B5228E >@30=V2 (203V=V2), A?@8G8=5=V 3@81818<8 (70728G09= @>4C *Candida*
), B0 AC?5@V=D5:FVW, A?@8G8=5=V <V:@>>@30=V7<0<8, GCB;828<8 4> :;>B@8<07>;;C.

@>B8?>:070==O.
V?5@GCB;82VABL 4> 4VNG>W @5G>28=8 B0 V=H8E :>@>=5=BV2 ?@5?0@0BC.

70AB>A>2C20B8 7 >AB5@56=VABN :V:0@AL:8<8 70A>10<8 B0 V=HV <5B>48 270T<>4VW.

@8 >4=>G0A=>AC20==V 7 ;0B5:A=8<8 :>=B@0F5?B820<8 <>65 A?@8G8=8=8B8 ?>H:>465==O >AB0==VE, B>=B@0F5?B82V2 <>65 7=86C20B8AO. 0FVT=B0< @@5:><5=4=>20=> 28:>@8AB>2C20B8 0;LB5@@=0B82=V <5B>48 :>=B@0F5?FVW ?@8=09 ?@>BO3>< 5 4=V2 ?VA;O 70AB>AC20==O FL>3> ?@5?0@0BC.
4=>G0A=5 ;V:C20==O 7 ::>B@@8<@07>;@>;><, I> 70AB>A>A2CTBLAO 203V=0;L=>, B0 B0:@@;V< ?5@@@0;;L=> (FK-506, VAC?@5A0@=B>=B) 01> AV@@@;V< <>65 ?@872>4@B8 4> ?V428I5==O @V2=O B0@:@@;V2V. "0:8< G8=>=><, A;V4 @5B@5;@L=> :>=B@@;N20B8 AB0@= E2@@@3@4 4;O 28O2;5==O A87C20==O B0@:@@;V AV@@@;VIEV4=>ABV H;OE=><< ?5@52V@:8 WE @V2==V2 C ?;072V.

A>1;82>AB8 70AB>AC20==O.
@@>BO3><< <5=AB@@C0FVW ;V:C20==O ?@@2>48B8 =5 A;V4. V:C20==O A;V4 70;V==G8B8 4> ?>G0B;:C <5=AB@@C0FVW.
%2>@V9 @5:>@<5=4CTBLAO ?@@:>=AC;LBC20B8AO 7 ;V:0@5O20E E2@@>@18; O:I> A8<<4 715@@V30NBLAO 4>2H5 7 4=V2; O:I> A8<<4 7O2;ONBLAO 7=>2C ?@@>BO3>< 2 5@54 ?@@>G0B;>@ 70AB>AC20==O A;V4 ?@@04@88AO 7 ;V:0@5<, O:I> C ?0FVT=B:8 28=8: 1C4L-O:89 7 =@0254=8E 40;V AB0B:2:
   - 3@@81:>20 V=D5:FVO ?@2B@@NTBLAO G0ABVH5, =V6 2 @@078 ?@@>BO3><< H5AB8
   - C ?0FVT=B:8 01> WW A@@1;52>@3> ?0@=B5@0 2 0=0=<=57V 1C;8 70E2@@@@N20==O, I> ?5@54@@0NBLAO AB0@528< H;OE=><;
   - ?0FVT=B:0 203VB=0 01> 203VB==0VABL ?V4>7@ONTBLAO;
   - ?0FVT=B:0 2V:>< 4> 12 01> 2V4 60 @@>:V2;
   - 2V4>@<0 3V7?@@GCB;82VABL 4> V;C 01> V=H8E 203V=0;L=8E ?@@B83@@81:>20V2.
5 @5:>=<5=4CTBLAO 157 ?@@048 ;V:0@O 70AB>A>A2CB8 ?@5?0@0B ?@@8:
   - =5@@53C;O@=;@>@8E 203V=0;L=8E :@@>2>2B5G;
   - 0=><0;L=8E 203V=0;L=8E :@@>2>2B5G G8 284@5;5==OE 73CAB:V2 :@@>2V;
   - A<5@4N?@8E 203V=0;L=8E 284V;5==OE;
   - 2C;L20@=;20;L=8E G8 203V=0;L=8E 28@@07:0E, CB2>@5==V
   - 1>;N 2 =86=V9 4V;O=FV 682>B0 G8 487C@@VW;
   - 1C4L-O:89 ?@@1VG5=8E 4V:5, B>;8E O: ?@@G5@@2=V==O, ?@@4@@07=5==O 01> =01@O:8,
      0A>@FV9>20=8E 7 ;V:C20==O<;
   - ?V428I5==V B5 ?@@?0A=FV;
   - =C4@@BV G8 1;N20==V;
   - 4V0@5W;
   - 1>;N C A?8=V;
   - 0A>@FV9>20=>N;N C ?;5G0E.
5:><5=4CTBLAO ;V:C20B8 2AV C@@065=V 4V;O=:8 H;OE=@< >4=>G0A=>.
#=8:09B8 :>=B0:BC 7 @G0<8 B0 =5 ?@@:>@2B0C20B8.
V4 G0A 70AB>AC20==O FL>3> ?@5?0@0BC A;V4 C=8:0B8 AB0@5528E :>=B0:BV2, >A:V;L:8 V=D5:FVO <>65 ?5@54052B8AO ?0@@B=5@@C. >65 7=86C20B8AO 5D5:B82VABL B0 157?5:0 ;0B5:A=8E :>=B@0F5?FV2 (B0:8E O: ?@575@20B828 B0 4V0D@03@<8).
A:V;L:8 728G09=> C@@6CNBLAO O: ?V@20, B0: V 7@2=VH=V AB0@528V >@30=8 (AB0@528V 3C18 B0 ?@8;53;V 4V;O=:8), A;V4 70AB>A>2C20B8 :>=1V=>20=> ;V:C20==O >1>E ?0@B=5@@V2, 2:;NG0NG8 V4 G0A ;V:C20==O ?@@5?0@0B@>< <5:@20 V7 70AB>AC20==O< :@@5 :0@5528E AB0@@528E 0@3@@5?@05=>4@B8=A B> ?5@54@@0NB8AO, 0:A5@0@3>
5 28:>@@8AB>2C20B8 B0:=8, V=B@@0203V=0;L=V 7@>;H5==O, A;V4 70AB>AC20B8 FL>3> ?@5?0@0BC.

0AB>AC20==O C ?5@@>4V 203VB=>ABV 01> 3>4C20==O 3@C44N.
;V=VG=V 4V0;V465==O I>4> 2@07:@82C :@>B5;AB2V< =0 D5@B8;L=VABL ;N4@8=8 =5 ?@@2>4@8;8AL, 0;5 ?@@>B5 4@O;V465==O =0 B20@8=0:E =5 28O28;8 2?;82C :@>B5;AB2V:. 0 B20@8=0:E =5 28O28;8 ?@@OC 2@82C 01> =5?@OC 2@@82C H:V4;82>3> 2?;82C 7 B>G:8 7 B0 B0;V2 B0 ?@@02@4>45==O. V;L=VABL 4@O;V4=L 7 28:>>G52==VH<< :@>B5;;L 7 28:@>G5==>< ?@>B2@0=8 ?@@5;55==O ?@@5?0@0BC ?@@>BO3>< I B>@8 <5=AB@@C0FVW.
V4 G0A 70AB>AC20==O ?@@5?0@0BC A;V4 ?@@8?8=8B8 3>4C20==O 3@C44N.

40B=VABL 2?;820B8 =0 H284:VABL @50:FVW ?@8 :5@C20==V 02B>B@0=A?>@B✕ 01> V=H8<8 <5E0=V7<0<8.

0=8E =5<0T.

!?>AV1 70AB>AC20==O B0 4>78.

0728G09 ?@5?0@0B A;V4 70AB>A>2C20B8 ?> 1 B01;5BFV 2 @078 =0 4>1C ?@@>BO3✕ 3 4=V2 01> ?> 1 B01;5BFV =0 4>1C ?@@>BO3✕ 6 4=V2.

;O ?>2=>3> @>7G8=5=O B01;5B8 C 203V=V ?>B@V1=5 2 @078 A5@@54>28I5, V=0:H5 =5@@@>7G8=5=V G0AB>:8 B01;5B8 <>6CBL 28A8?0B8AO =07>2=V. ;O 70?>1V30==O FL>48B8 O:><>3> 3;81H5 C 203V=C 1060=> ?5@54 A=>

V:C20==O A;V4 7025@H8B8 4> ?>G0B:C<5=AB@C0FVW. V4 G0A<5=AB@C0FVW ;V:C20==O ?@@>2>48B8 =5 A;V4 G5@57 @878: 28<820==O ?@5?0@0BC <5=AB@C0;L=8<8 284V;5==O<8.

5 28>?@8AB>2C20B8 B0=8, V=B>@0203V=0;L=V 7@@>H5=O, A?5@ V=HV 203V=0;L=V ?@@>4C:B8 ?V4 G0A 70AB>AC20==O FL>3> ?@5?0@0BC.

VB8.

@5?0@0B =5 @5;V:=5=4CTBLAO 70AB>A>2C20B8 4VB8< 2V:✕ 4> 12 @>:V2. VB8< 2V:✕ 2V4 12 @>:V2 70AB>A>2C20B8 ?VA;O :>=AC;LB0FVW 7 ;V:0@5

5@54>7C20==O.

>4=>3> @878:C 3>AB@@>W V=B>:A8:0FVW =5<0T, >A:V;L:8<0<>9<>2@@>=, I> ?5@54>7C20==O <>6;825 ?VA;O @07>2>W 203V=0;L=>W 4>78, 0 B0>6 ?VA;O 28@@>2>3> ?5@54>7C20==O. !?5F8F8G=>3> 0=B84>BC =5 VA=CT. @8 28@@>2>@0;L=><C ?5@54>7C20==V @V4> <>65 28=8:=CB8 ?>B@@>510 C ?@@>2545==V ?@@><820==O H;C=:0, O:I> 4>70, >0 703@@>6CT 68BBN, 1C;0 70AB>A>20=0 ?@>BO3✕ ?>?5@54=L>W 3>48=8 01> O:I> =0O2=V 2848

>1VG=V @50:FVW.

1>:C VW A8AB5<8: 0;5@3VG=V @50:FVW, 2:;NG0NG8 :@@>?82O=:C, 48A?=>5, 0@B5@V0;L=C 3V?>B5=5V7VN, A8>:=5V.

1>:C H;C=:@>2>-:8H:@>2@@>3> B@@>0:BC: 1V;L C 682@>BV.

1>:C @5?@@>4C:B82=>W A8AB5<8: 48A>B>@B C 4V;O=FV 203V=8, =01@O:, 2V4GCBB O ?5G5==O, 5@8B5<0, ;CI5==O C 4V;O=FV 35=VB0;VW, ?>4@07=5==O, A25@1V6, 1V;L C B>;>2V9 4V;O=FV, 28A8?0==O, 203V=0;L=0 :@@>2>B5G0.

"5@ABV. 3 @>:8.

#<>28 715@V30==O. 15@V30B8 C =54>ABC?=><

#?0:>2:0. 6 B01;5B>: C %/0;N==C C C?0:>2:C.

0B53>@VO 2V4?CA:C. 57 @5F5?B0.

8@>1=8:. ;0:A>!
GlaxoSmithKline Pharmaceuticals S.A., Poland.

VAF57=0E>465==O 28@@>1=8:0 B0 9>3> 04@5A0 20465==O 4VO;L=>ABV. ;0:A>!
189, 2C;. @N=20;L4AL:0, 60-322 >7=0=L, >;LI0/
GlaxoSmithKline Pharmaceuticals S.A.
189 Grunwaldzka Str., 60-322 Poznan, Poland.