

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

!;:04:

4VNG0 @5G>28=0: tamsulosin;

1 :0?AC;0 B078=C 3V4@>E;>@84C (C 283;04V B078=C 3V4@>E;>@84C 0,15 % ! , ?5;5B) 0,4 <3;
4>?>28=8: FC:>@ AD5@8G=89, 5B8;F5;N;>70, 3V4@>:A8?@>?V;<5B8;F5;N;>70, ?>2V4=>, 3V?@>
<5;>78 DB0;0B, A?8@B F5B8;>289, 4V5B8;DB0;0B, B0;L;;
A.;:04 B25@4>W 65;0B8=>2>W :0?AC;8: 65;0B8=, 70;V70 >:A84 G5@2>=89 (172), 70;V70 >:A84 6>2B89
(172), B8B0=C 4V>:A84 (171), 10@2=8: V=483>B8= (132).

V:0@AL:0 D>@<0. 0?AC;8 7 <>48DV:>20=8< 282V;L=5==O<, B25@4V.

A=>2=V DV78:>-EVABV: :0?AC;8 B25@4V 65;0B8=>2V 2, V7 :@8H5G:>N A2VB;>-75;5=>3> :>;L>@C V
>@?CA>< >@0=652>3> :>;L>@C. 3> 01> <0965 1V;>3> :>;L>@C.

\$0@<0:>B5@0?52B8G=0 3@C?0. 0A>18, I> 70AB>A>2CNBLAO ?@8 4>1@>O:VA=V9 3V?5@?;07VW
?5@542>W 70;>78. =B03>=VAB8 α₁-04@5=>5@3VG=8E @5F5?B>@V2. >4 "% G04C A02.

\$0@<0:>;>3VG=V 2;0AB82>ABV.

\$0@<0:>48=0

45=>@< 281V@:>2> V :=:C@5=B=> 1;>;CT ?>ABA8=0?B8G=V α₁-04@5=>@5F5?B>@8, 7>:@5<0 α₁A
B0 α₁D, I> 7=0E>4OBLAO 2 3;04:V9 2>W 70;>78, H89:8 A5G>2>3> AB0B8G=>W G0AB8=8 C@5B@8.
&5 ?@872>48BL 4> 7=865==O B>=CAC 3;04:>W 2>W 70;>78, H89:8 A5G>2>3> AB0B8G=>W G0AB8=8
C@5B@8 B0 ?>;V?H5==O 284V;5==O A5GV. 4=>G0A=> 7-5=HCNBLAO A8<8 >1AB@C:FVW B0
?>4@07=5==O, ?>2O70=V 7 4>1@>O:VA=>N 3V?5@?;07VTN ?5@542>W 70;>78 (CB@C4=5==O
?>G0B:C A5G>28?CA:0==O, ?>A;01;5==O AB@C<5=O A5GV, :@0?0==O ?VA;O 70:V=G5==O
A5G>28?CA:0==O, 2V4GCBBO =5?>2=>3> A?>@>6=5==O A5G>2>3> 7828 4> A5G>28?CA:0==O, ?>7828
4> A5G>28?CA:0==O 2 =VG=89 G0A, =52V4;:04=VABL A5G>28?CA:0==O).

/: ?@028;>, B5@0?52B8G=89 5D5:B @>72820TBLAO G5@57 2 B86=V 2V4 ?>G0B:C ?@89>2389 G0A
715@V30NBLAO ?@8 4>23>AB@:>2>N N AB@82545==O EV@C@3VG=>W >?5@0FVW 01>
:0B5B5@870FVW.

=B03>=VAB8 α₁-04@5=>@5F5?B>@V2 <0NBL 740B=VABL 7=86C20B8 0@B5@V0;L=89 B8A: H;OE×
7=865==O ?5@8D5@8G=>3> B>=CAC AC48=. V4 G0A ?@>2545==O 28?@>1C20=L?@5?0@0BC 45=>@<
=5 2V47=0G0;>AO ;:V=VG=> 28@065=>3> 7=865==O 0@B5@V0;L=>3> B8A:C.

\$0@<0:>:V=5B8:0.

A<>:BC20==O. "078= 4>1@5 2A<>:BCTBLAO 7V H:C=:>2>.:8H:>2>3> B@0:BC, 0 9>3>

1V>4>ABC?=VABL AB0=>28BL <0965 100 %. A<>:BC20==O B078=C 2V41C20TBLAO 45I> ?>2V;L=VH5
?VA;O ?@89>@V4=VABL 2A<>:BC20==O 4>AO30TBLAO 2 B>@07V, :>;8 ?0FVT=B ?@89<0T □45=>@<
2 >48= V B>9 A0<89 G0A ?VA;O ?@89>78=C <0T ;V=V9=89 E0@0:B5@.

VA;O ?@89>2>W 4>78 ?@5?0@0BC ?VA;O W6V ?V:>20 :==F5=B@0FVO B078=C C ?;072V
4>AO30TBLAO ?@81;87=> G5@57 6 3>48=, 0 AB01V;L=0 :==F5=B@0FVO CB2>@NTBLAO =0 ?OBC
4>1C ?VA;O I>45=>3> ?@89>C_{max} ?@8 FL> =0 42V B@5B8=8 28I>N 70 BC, I> CB2>@NTBLAO ?VA;O
?@89>2>W 4>78.

>7?>4V;. # G>;>2V:V2 B078= ?@81;87=> =0 99 % 7207CTBLAO 7 1V;:0<8 ?;07<8. 1T< @>7?>4V;C
?@5?0@0BC =57=0G=89 (?@81;87=> 0,2 ;/:3).

5B01>;V7<. "078=C 3V4@>E;>@84 =5 ?V440TBLAO 5D5:BC ?5@H>3> ?@>E>465==O V ?>2V;L=>
<5B01>;V7CTBLAO 2 ?5GV=FV 7 CB2>@5==O< D0@<0:>;>3VG=> 0:B82=8E <5B01>;V8V2, I>
715@V30NBL 28A>:C A5;5:B82=VABL 4> α₁-04@5=>@5F5?B>@V2. V;LH0 G0AB8=0 0:B82=>W
@5G>28=8 ?@8ACB=O 2 :@>2V 2 =57

;V. "078= B0 9>3> <5B01>;V8 282>4OBLAO 7 >@30=V7 V7 A5G5N. @81;87=> 9 % 4>78 70;8H0TBLAO
C 283;04V =57W 4VNG>W @5G>28=8.

VA;O @07>2>3> ?@89>78 ?@5?0@0BC ?VA;O W48 B0 ?@8 AB01V;L=V9 :==F5=B@0FVW 2 ?;072V
?5@V>48 =0?V2282545==O AB0=>2;OBL ?@81;87=> 10 B0 13 3>48= 2V4?>2V4=>.

;V=VG=V E0@0:B5@8AB8:8.

>:070==O.

V:C20==O DC=:FV>=0;L=8E @>7;04V2 7 1>:C =86=VE A5G>282V4=8E H;OE2 ?@84>1@>O:VA=V9 3V?5@?;07VW ?@>AB0B8.

@>B8?>:070==O.

V?5@GCB;82VABL 4> B078=C 3V4@>E;>@84C, 2;;NG0NG8 <548:0<5=B>7=>-V=4C:>20=89 0=3V>=52@>B8G=89 =01@O:, 01> 4> 1C4L-O:>W 7 4>?>28=; =0O2=VABL 2 0=0<=57V >@B>AB0B8G=>W 3V?>B5=7VW; BO6:0 ?5GV=:>20 =54>AB0B=VABL.

70T<>4VO 7 V=H8<8 ;V:0@AL:8<8 70A>10<8 B0 V=HV 2848 270T<>4V9.

>A;V465==O 270T<>4VW ?@>2>48;8 BV;L:8 C 4>@>A;8E.
@8 >4=>G0A=>AC20==V B078=C 3V4@>E;>@84C 7 0B5=>;>;<, 5=0;0?@8;< 01> B5>DV;V=<<
;V:0@AL:>W 270T<>4VW =5 2V47=0G0;>AO. 4=>G0A=5 70AB>AC20==O 7 F8<5B848=>< ?V428ICT, 0 7
DC@>A5< 7=86CT :>=F5=B@0FVN B078=C C ?;072V, 0;5 >A:V;L:8 FV @V2=V 70;8H0NBLAO 2<560E
=>@<8, C A?5FV0;L=V9 :>@5:FVW 4>7C20==O B078=C =5<0T ?>B@518.
0O2=V 40=V A2V4G0BL, I> 4V075?0<, ?@>?@0=>;>;, B@8E;>@<5BV0784, E;>@<048=>=, 078=C C ?;07
2V ;N48=8. >4V1=8< G8=>< B078= =5 7?@0=>;>;C, B@8E;>@<5BV0784C B0 E;>@<048=>=C C ?;072V
;N48=8.

@>B5 48;>D5=0: B0 20@D0@8= <>6CBL ?V428IC20B8 H284:VABL 5;V78=C.
4=>G0A=5 70AB>AC20==O B078=C 3V4@>E;>@84C 7 A8;L=8<8 V=3V1VB>@0<8 CYP3A4 <>65
?@8725AB8 4> 71V;LH5==O 2?;82C B078=C 3V4@>E;>@84C. 4=>G0A=5 70AB>AC20==O 7
:5B>:>=07>;< (2V4><89 A8;L=89 V=3V1VB>@ CYP3A4) ?@872>48;> 4> 71V;LH5==O AUC V !max
4>
2,8 V 2,2 2V4?>2V4=>.

"078=C 3V4@>E;>@84 =5 A;V4 ?@87=0G0B8 C :<1V=0FVW 7 A8;L=8<8 V=3V1VB>@0<8 CYP3A4
?0FVT=B0< 7 =87L:8< <5B01>;V7<< CYP2D6.
"078=C 3V4@>E;>@84 A;V4 70AB>A>2C20B8 7 >15@56=VABN C :<1V=0FVW 7 A8;L=8<8 V ?>
4=>G0A=5 70AB>AC20==O B078=C 3V4@>E;>@84C V ?0@>:A5B8=C (A8;L=89 V=3V1VB>@ !YP2D6)
?@872>48BL 4> 71V;LH5==O !max V AUC 4> 1,3 V 1,6 2V4?>2V4=>, 0;5 F5 =5 T ;;V=VG=> 7=0GCI8
4=>G0A=5 70AB>AC20==O 7 V=H8<8 α_1 -04@5=>1;>;:0B>@0<8 <>65 ?>A8;N20B8 3V?>B5=782=89 5D5:B.

A>I;82>ABV 70AB>AC20==O.

/: V ?@8 70AB>AC20==V V=H8E α_1 -04@5=>1;>;:0B>@V2, 2 >:@5<8E 28?04:0E ?@8 70AB>AC20==V
;V:0@AL:>3> 70A>1C 45=>@< <>6;825 7=865==O 0@B5@V0;L=>3> B8A:C, I> <>65 V=>4V ?@8725AB8
4> 2B@0B8 A2V4>>ABV. @8 ?>O2V ?5@H8E >7=0: >@B>AB0B8G=>W 3V?>B5=7VW (70?0
<>@>G5==O, A;01:VABL) ?0FVT=B<0T ?@8AVAB8 01> ?@89=OB8 3>@87>=B0;L=5 ?>;>65==O 4>
7=8:=5==O 28I573040=8E A8
5@54 B8< O: @>7?>G0B8 ;V:C20==O ;V:0@AL:8< 70A>1><< 45=>@<, A;V4 ?@>9B8 <548G=5
>1AB565==O 7 <5B>N 28O2;5==O V=H8E AC?CB=VE 70E2>@N20=L, I> <>6CBL A?@8G8=8B8 B0:V A0
2>W 70;>78. 5@54 ?>G0B:<< ;V:C20==O =5>1EV4=> ?@>25AB8 @5:B0;L=5 >1AB565==O ?5@542>W
70;>78 B0 C @07V =5>1EV4=>ABV B5AB =0 287=0G5==O @V2=O A?5F8DVG=>3> 0=B835=C ?5@54
2>W 70;>78 (PSA) 4> ?>G0B:C B0 G5@57 >4=0:>2V ?@>
@87=0G0B8 ;V:0@AL:89 70AV1 ?0FVT=B0< V7 BO6:>N D>@<>N =8@:>2>W =54>AB0B=>ABV
(;V@5=A :@50B8=V=C <10 <;/E2) =5>1EV4=> 7 >A>1;82>N >15@56=VABN, >A:V;L:8 ;;V=VG=8E
4>A;V465=L V7 70AB>AC20==O ;V:0@AL:>3> 70A>1C B0:8< ?0FVT=B0< =5 ?@>2>48;8.
450:8E ?0FVT=BV2, O:V 70AB>A>2C20;8 B078=, ?V4 G0A EV@C@3VG=>3> 2B@CG0==O 7 ?@82>4C
:0B0@0:B8 V 3;0C:<<8 2V47=0G02AO A8=4@<< 0B>=VG=>W 7V=8FV (IFIS, 20@V0=B A8=4@>W
7V=8FV), I> <>65 AB0B8 ?@8G8=>N 71V;LH5==O :V;L:>ABV CA::04=5=L ?V4 G0A 01> ?VA;O
?@>2545==O B0:>W >?5@0FVW.
/: ?@028;>, 70 1-2 B86=V ?5@54 ?@>2545==O< >?5@0FVW 7 ?@82>4C :0B0@0:B8 V 3;0C:<<8 @5:>
<5=4CTBLAO ?@878=8B8 ;V:C20==O B078=><, ?@>B5 :>@8ABL 2V4 ?@878=5==O ;V:C20==O B078=><
=0 AL>3>4=VH=V9 45=L B>G=> =5 2AB0=>2;5=0. >2V4><;O;>AL B0:>6 ?@> A8=4@<< 0B>=VG=>W
7V=8FV ?>2V4><;O;>AO B0:>6 C ?0FVT=BV2, O:V ?@878=8;8 70AB>AC20==O B078=C 704>23> 4>
?@>2545==O >?5@0B82=>3> 2B@CG0==O 7 ?@82>4C :0B0@0:B8.

0FVT=B0< ?5@54 ?;0=>2>N >?5@0FVTN 7 ?@82>4C :0B0@0:B8 01> 3;0C:><8 =5 @5:><5=4CTBLAO @>7?>G8=0B8 70AB>AC20==O B078=C 3V4@>E;>@84C. @8 ?V43>B>2FV 4> >?5@0FVW EV@C@38 B0 >DB0;L<>;>38 <0NBL 4V7=0B8AO, G8 70AB>A>2C202 (01> 70AB>A>2CT) ?0FVT=B B078=, 7 <5B>N ?>?5@5465==O <>6;828E CA;;04=5=L, ?>2O70=8E V7 IFIS.

"078=C 3V4@>E;>@84 =5 A;V4 ?@87=0G0B8 C :><1V=0FVW 7 A8;L=8<8 V=3V1VB>@0<8 CYP3A4 ?0FVT=B0< 7 =87L:8< <5B01>;V7<<< CYP2D6.

"078=C 3V4@>E;>@84 A;V4 70AB>A>2C20B8 7 >15@56=VABN C :><1V=0FVW 7 A8;L=8<8 V ?> «□70T <>4VO 7 V=H8<8 ;V:0@AL:8<8 70A>10<8 B0 V=HV 2848 270T<>4V9»).

V4>78= C ?0FVT=BV2 7 =0O2=VABN 2 0=0<=57V 0;5@3VW =0 AC;LD0=V;0B@815@56=>ABV ?@8 70AB>AC20==V B078=C 3V4@>E;>@84C ?0FVT=B0<, C O:8E @0=VH5 2V4

0AB>AC20==O C ?5@V>4 203VB=>ABV 01> 3>4C20==O 3@C44N.

45=>@< =5 ?>:070=89 4;O 70AB>AC20==O 6V=:0

\$5@B8;L=VABL

0O2=V 40=V A2V4G0BL, I> ?V4 G0A 70AB>AC20==O B078=C A?>AB5@V30;8AO 28?04:8 ?>@CH5==O 5O:C;OFVW, @5B@>3@04=>W 5O:C;OFVW V =54>AB0B=L>W 5O:C;OFVW.

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

>A;V465==O ??;82C ?@5?0@0BC =0 740B=VABL :5@C20B8 02B>B@0=A?>@B< 01> <5E0=V7<0<8 =5 ?@>2>48;8AO. 4=0: ?0FVT=BV2 ?>B@V1=> ?>?5@548B8 ?@> <>6;82VABL 28=8:=5==O 70?0 <>@>G5==O.

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

5:><5=4>20=0 4>70 4;O 4>@>A;8E 1 :0?AC;0 I>45==>, ?VA;O A=V40=C; :0?AC;C A;V4 :>2B0B8 FV;>N 7 <>;>:> 01> 2>4>N (?@81;87=> 150 <;), AB>OG8 01> A84OG8; :0?AC;C ?@89<0B8 FV;>N, =5 @>7 6>2C20B8, >A:V;L:8 F5 1C45 ?5@5H:>460B8 <>48DV:>20=>3> V=3@54VT=B0.

VB8.

V:0@AL:89 70AV1 =5 70AB>A>2C20B8 4VBO

57?5:0 B0 5D5:B82=VABL 70AB>AC20==O B078=C 4;O 4VB59 (4> 18 @>:V2) =5 >FV=N20;0AO.

5@54>7C20==O.

!8<8.

5@54>7C20==O B078=C 3V4@>E;>@84<< <>65 A?@8G8=8B8 BO6:C 3V?>B5=782=C 4VN. "O6:0 3V?>B5=782=0 4VO 2V47C20==O.

V:C20==O.

28?04:C @V7:>3> 7=865==O B8A:C 2=0A;V4>: ?5@54>7C20==O A;V4 ?@>2>48B8 ?V4B@8: 28A>:>3> ABC?5=O 72O7C20==O B078=C 7 1V;;<8 ?;07<8 ?@>2545==O 35<>4V0;V7C =02@O4 G8 T 4>FV;L=8 <5B>N ?@8?8=5==O ?>40;LH>3> 2A<>:BC20==O ;V:0@AL:>3> 70A>1C <>6=0 HBCG=> 28;;8:0B8 1;N20==O. @8 ?5@54>7C20==V 7=0G=>N :V;L:VABN ;V:0@AL:>3> 70A>1C ?0FVT=BC =5>1EV4=> ?@> <8B8 H;C=>: V7 70AB>AC20==O< 0:B82>20=>3> 2C3V;;O B0 =87L:>>A<>B8G=8E ?@>=>A=8E 70A>1V2, B0:8E O: AC;LD0B =0B@VN.

>IVG=V @50:FVW.

I>:C =5@2>2>W A8AB5<8: 70?0<>@>G5==O; 3>;>2=89 1V;L; =5?@8B<=VABL.

I>:C >@30=V2 7>@C: 70BC<0=5==O 7>@C, ?>@CH5==O 7>@C.

I>:C A5@F52>-AC48==>W A8AB5<8: 2V4GCBBO A5@F518BBO; >@B>AB0B8G=0 3V?>B5=7VO.

5A?V@0B>@=>-<54V0AB8=0;L=V @>7;048: @8=VB; =>A>20 :@>2>B5G0.

I>:C H;C=:>2>-:8H:>2>3> B@0:BC: 70?>@, 4V0@5O, =C4>B0, 1;N20==O.

I>:C H:V@8 B0 A;87>28E >I>;>=>:: 28A8?, A25@1V6, :@>?82O=:0; 0=3V>=52@>B8G=89 =01@O;;

A8=4@<< !BV25=A0 - □6>=A>=0; @<=0 5@8B5<0, 5:AD>;V0B82=89 45@<0B8B.

I>:C AB0B52>W A8AB5<8: @>7;048 5O:C;OFVW, 2;;NG0NG8 @5B@>3@04=C 5O:C;OFVN V =54>AB0B=VABL 5O:C;OFVW.

030;L=V @>7;048: 0AB5=VO.

?8A0=V 28?04:8 V=B@0>?5@0FV9=>W =5AB01V;L=>ABV @094C6=>W >1>;>=:8 >:0 (A8=4@< 72C65=>W 7V=8FV) ?@8 >?5@0FVW 7 ?@82>4C :0B0@0:B8 V 3;0C:><8 C ?0FVT=BV2, O:V 70AB>A>2C20;8 B078= (482. @>74V; «A>1;82>ABV 70AB>AC20==O»).

@V< 28I52:070=8E ?>1VG=8E @50:FV9, ?>2V4<;O;>AO ?@> 28?04:8 DV1@8;OFVW ?5@54A5@4L, 0@8B5, G0AB>B0 28=8:=5==O O:8E =5 <>65 1CB8 4>AB>2V@=> 2AB0=>2;5=0.

"5@ABV.3 @>:8.

#<>28 715@V30==O.

15@V30B8 2 >@83V=0;L=V9 C?0:>2FV ?@8 B5
15@V30B8 C =54>ABC?=>

#?0:>2:0.

> 10 :0?AC; C 1;VAB5@V; ?> 3 1;VAB5@8 C ?0GFV.

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

8@>1=8:. " «8W2AL:89 2VB04».

VAF57=0E>465==O 28@>1=8:0 B0 9>3> 04@5A020465==O 4VO;L=>ABV.

04073, #: @0W=0, ?8;V2AL:0, 38.

Web-A09B: www.vitamin.com.ua.

!" #&/

?> <548F8=A:>;5:0@AB25==>3> A@54AB20

(ADENORM)

!>AB02:

459AB2CNI55 25I5AB2>: tamsulosin;

1 :0?AC;0 A>45@68B B078=0 384@>E;>@840 (2 2845 B078=0 384@>E;>@840 0,15 % ! , ?5;;5B) 0,4 <3;
2A?><>30B5;L=K5 25I5AB20: A0E0@ AD5@8G5A:89, MB8;F5;;N;>70, 384@>:A8?@>?8;<5B8;F5;;N;>70,
?>284=>, 38?@><5;;>7K DB0;0B, A?8@B F5B8;>2K9, 48MB8;DB0;0B, B0;L;;
A>AB02 B25@4>9 65;0B8=>2>9 :0?AC;K: 65;0B8=, 65;570 >:A84 :@0A=K9 (172), 65;570 >:A84 65;BK9
(172), B8B0=0 48>:A84 (171), :@0A8B5;L 8=483>B8= (132).

5:0@AB25==0O D>@<0. 0?AC;K A <>48D8F8@>20==K< 2KA2>1>645=85<, B25@4K5.

A=>2=K5 D878:>-E8<8G5A:85 A2>9AB20: :0?AC;K B25@4K5 65;0B8=>2K5 2, A :@KH5G:>9 A25B;>-
75;5=>3> F25B0 8 :>@?CA<< >@0=652>3> F25B0. !>45@68<>5 :0?AC; AD5@8G5A:85 ?5;;5BK 15;>3> 8;8
?>GB8 15;>3> F25B0.

\$0@<0:>B5@0?52B8G5A:0O 3@C??0. !@54AB20, ?@8<5=ONI85AO ?@8 4>1@>:0G5AB25==>9

38?5@?;0788 ?@54AB0B5;L=>9 65;57K. =B03>=8ABK α₁-04@5=5@38G5A:8E @5F5?B>@>2.

>4 "% G04C A02.

\$0@<0:>;>38G5A:85 A2>9AB20.

\$0@<0:>48=0<8:0.

45=>@< 8718@0B5;L=> 8 :>=:C@5=B=> 1;>:8@C5B ?>ABA8=0?B8G5A:85 α₁-04@5=>@5F5?B>@K, 2
G0AB=>AB8 α₁A 8 α₁D, :>B>@K5 =0E>4OBAO 2 3;04:>9 9 65;57K, H59:8 <>G52>3> ?C7K@O 8
?@>AB0B8G5A:>9 G0AB8 C@5B@K. -B> ?@82>48B : A=865=8N B>=CA0 3;04:>9 ?@54AB0B5;L=>9
65;57K, H59:8 <>G52>3> ?C7K@O 8 ?@>AB0B8G5A:>9 G0AB8 C@5B@K, 0 B0:65 C;CGH5=8N
<>G5>B45;5=8O. 4=>2@5<5==> C<5=LH0NBAO A81AB@C:F88 8 @074@065=8O, A2O70==K5 A
4>1@>:0G5AB25==>9 38?5@?;07859 ?@54AB0B5;L=>9 65;57K (70B@C4=5=85 =0G0;0
<>G58A?CA:0=8O, >A;01;5=85 AB@C8 <>G8, :0?0=85 ?>A;5 >:=G0=8O <>G58A?CA:0=8O, >ICI5=85
=5?>;=>3> >?>@>6=5=8O <>G52>3> ?C7K@O, G0ABK5 ?>7K2K : <>G58A?CA:0=8N, ?>7K2K :

<>G58A?CA:0=8N 2 =>G=>5 2@5B;>6=>ABL <>G58A?CA:0=8O).
0: ?@028;>, B5@0?52B8G5A:89 MDD5:B @0728205BAO G5@57 2 =545;8 >B =0G0;0 ?@85<0
?@5?0@0B0. -B8 MDD5:BK 4;8B5;L=>5 2@5E@0=ONBAO ?@8 4>;3>A@>G=><< ;5G5=88 8 2
7=0G8B5;L=>9 AB5?5=8 A45@6820NB ?@>2545=85 E8@C@38G5A:>9 >?5@0F88 8;8 :0B5B5@870F88.
=B03>=8ABK α_1 -04@5=>@5F5?B>@>2 A?>A>1=K A=860BL 0@B5@80;L=>5 402;5=85 ?CB5< A=865=8O
?5@8D5@8G5A:>3> B>=CA0 A>AC4>2. > 2@52545=8O 8A?KB0=89 ?@5?0@0B0 45=>@< =5 >B
<5G0;>AL ::8=8G5A:8 2K@065=>3> A=865=8O 0@B5@80;L=>3> 402;5=8O.

\$0@<0:>:8=5B8:0.
A0AK20=85. "078= E>@>H> 2A0AK205BAO 87 65;C4>G=>-.:8H5G=>3> B@0:B0, 0 53>
18>4>ABC?=>ABL A>AB02;05B ?>GB8 100 %. A0AK20=85 B078=0 ?@>8AE>48B =5A:>;L:> <54;5==55
?>A;5 ?@85<0 ?8I8. 4=>@>4=>ABL 2A0AK20=8O 4>AB8305BAO 2 B<< A;CG05, :>340 ?0F85=B ?@8=8
<05B □45=>@< 2 >4=> 8 B> 65 2@5A;5 ?@85<0 ?8I8. \$0@<0:>:8=5B8:0 B078=0 =>A8B ;8=59=K9
E0@0:B5@.

>A;5 ?@85<0 @07>2>9 4>7K ?@5?0@0B0 ?>A;5 54K ?8:>20O :>=F5=B@0F8O B078=0 2 ?;07<5 :@>28
4>AB8305BAO ?@81;878B5;L=> G5@57 6 G0A>2, 0 AB018;L=0O :>=F5=B@0F8O 2>7=8:05B =0 ?0BK5
ACB:8 ?>A;5 5654=52=>3> ?@85<0 ?@5?0@0B0. C_{max} ?@8 MB<< ?@81;878B5;L=> =0 425 B@5B8 2KH5
B>9, :>B>@0O 2>7=8:05B ?>A;5 ?@85<0 @07>2>9 4>7K.

0A?@545;5=85. # 78= ?@81;878B5;L=> =0 99 % A2O7K205BAO A 15;:0<8 ?;07
5B01>;87"078=0 384@>E;>@84 =5 ?>4405BAO MDD5:BC ?5@2>3> ?@>E>645=8O 8 <54;5==>
<5B01>;878@C5BAO 2 ?5G5=8 A >1@07>20=85< D0@<0:>;>38G5A:8 0:B82=KE <5B01>;8B>2, :>B>@K5
A>E@0=ONB 2KA>;CN A5;5:B82=>ABL : α_1 -04@5=>@5F5?B>@0;LH0O G0ABL 0:B82=>3> 25I5AB20
?@8ACB2C5B 2 :@>28 2 =587<5=5==>< 2845.

-;8<8=0F8O. "078= 8 53> <5B01>;8BK 2K2>4OBAO 87 >@30=87<0 ?@58 A <>G>9. @81;878B5;L=> 9 %
4>7K >AB05BAO 2 2845 =587<5=5==>3> 459AB2CNI53> 25I5AB20.

>A;5 @07>2>3> ?@85<0 4>7K ?@5?0@0B0 ?>A;5 54K 8 ?@8 AB018;L=>9 :>=F5=B@0F88 2 ?;07<5 :@>28
?5@8>4K ?>;C2K2545=8O A>AB02;ONB ?@81;878B5;L=> 10 8 13 G0A>2 A>>B25BAB25==>.

**;8=8G5A:85 E0@0:B5@8AB8:8.
>:070=8O.**

5G5=85 DC=:F8>=0;L=KE =0@CH5=89 A> AB>@>=K =86=8E <>G52K45;8B5;L=KE ?CB59 ?@8
4>1@>:0G5AB25==>9 38?5@?;0788 ?@>AB0BK.

@>B82?>:070=8O.

8?5@GC2AB28B5;L=>ABL : B078=0 384@>E;>@84C, 2;:NG0O <548:0<5=B>7=>-8=4CF8@>20==K9
0=38>=52@>B8G5A:89 >B5.; 8,8 : ;N1<<30B5;L=KE 25I5AB2; =0;8G85 2 0=0<=575 >@B>AB0B8G5A:>9
38?>B5=788; B065;0O ?5G5=>G=0O =54>AB0B>G=>ABL.

708<>459AB285 A 4@C38<8 ;5:0@AB25==K<8 A@54AB20<8 8 4@C385 284K 2708<>459AB289.

AA;54>20=8O 2708<>459AB28O ?@>2>48;8AL B>;L:> C 27@>A;KE.
@8 >4=>2@5<5==>< ?@8<5=5=88 B078=0 384@>E;>@840 A 0B5=>;>;<, M=0;0?@8;< 8;8 B5>D8;;8=><
>5:0@AB25==>3> 2708<>459AB28O =5 >B<5G0;>AL. 4=>2@5<5==>5 ?@8<5=5=85 A F8<5B848=><<
?>2KH05B, 0 A DC@>A5<84>< A=8605B :>=F5=B@0F8N B078=0 2 ?;07<5 :@>28, => B0: :0: MB8
C@>2=8 >AB0NBAO 2 ?@545;0E =>@9 :>@@5:F88 4>78@>2:8 B078=0 =5B =5>1E>48<>AB8.
<5NI85AO 40==K5 A2845B5;LAB2CNB, GB> 48075?0<, ?@>?@0=>;>;, B@8E;>@<5B80784, E;>@
<048=>=, 0<8B@8?B8;8=, 48;:>D5=0.; 3;815=;:0<84, A8<20AB0B8= 8 20@D0@8= =5 2;8ONB =0
A2>1>4=CN D@0:F8N B078=0 2 ?;07<5 :@>28 G5;>25:0. >4>1=K<>1@07<< B078= =5 87<5=O5B
C@>25=L A2>1>4=KE D@0:F89 48075?0<, ?@>?@0=>;>;0, B@8E;>@<5B807840 8 E;>@<048=>=0 2 ?;07
<5 :@>28 G5;>25:0.

4=0:> 48;:>D5=0: 8 20@D0@8= <>3CB ?>2KH0BL A:>@>ABL M;8<8=0F88 B078=0.
4=>2@5<5==>5 ?@8<5=5=85 B078=0 384@>E;>@840 A A8;L=K<8 8=3818B>@0<8 CYP3A4 <>65B
?@825AB8 : C25;8G5=8N 2;8O=8O B078=0 384@>E;>@840. 4=>2@5<5==>5 ?@8<5=5=85 A :5B>:>=07>;>
< (8725AB=K9 A8;L=K9 8=3818B>@ CYP3A4) ?@82>48;> : C25;8G5=8N AUC 8 !_{max} 4> 2,8 8 2,2
A>>B25BAB25==>.

"078=0 384@>E;>@84 =5 A;54C5B =07=0G0BL 2 :<18=0F88 A A8;L=K<8 8=3818B>@0<8 CYP3A4
?0F85=B0< A =87:8< <5B01>;87<<< CYP2D6.

"078=0 384@>E;>@84 A;54C5B ?@8<5=OBL A >AB>@>6=>ABLN 2 :<18=0F88 A A8;L=K<8 8 C
<5@5==K<8 8=3818B>@0<8 CYP3A4.
4=>2@5<5==>5 ?@8<5=5=85 B078=0 384@>E;>@840 8 ?0@>:A5B8=0 (A8;L=K9 8=3818B>@ !YP2D6)
?@82>48B : C25;8G5=8N !max 8 AUC 4> 1,3 8 1,6 A>>B25BAB25==>, => MB> =5 O2;O5BAO :;8=8G5A:8
7=0G8
4=>2@5<5==>5 ?@8<5=5=85 A 4@C38<8 α₁-04@5=>1;:>:0B>@0<8 <>65B CA8;820BL 38?>B5=782=K9
MDD5:B.

A>15==>AB8 ?@8<5=5=80.

0: 8 ?@8 ?@8<5=5=88 4@C38E α₁-04@5=>1;:>:0B>@>2, 2 >B45;L=KE A;CG0OE ?@8 ?@8<5=5=88
>5:0@AB25==>3> A@54AB20 45=>@< 2>7<>6=> A=865=85 0@B5@80;L=>3> 402;5=8O, GB> <>65B
8=>340 ?@825AB8 : ?>B5@5 A>7=0=8O. @8 ?>O2;5=88 ?5@2KE ?@87=0:>2 >@B>AB0B8G5A:>9
38?>B5=788 (3>:>2>:@C65=85, A;01>ABL) ?0F85=B 4>;65= ?@8A5ABL 8;8 ?@8=OBL 3>@87>=B0;L=>5
?>;>65=85 4> 8AG57=>25=8O 2KH5C:070==KE A8<>2.
5@54 B5< :0=0G0BL ;5G5=85 ;5:0@AB25==K< A@54AB2<< 45=>@<, A;54C5B ?@>9B8 <548F8=A:>5
>1A;54>20=85 A F5;LN>1=0@C65=8O 4@C38E A>?CBAB2CNI8E 701>;520=89, :>B>@K5 <>3CB
2K720BL B0:85 65 A81@>:0G5AB25==0O 38?5@?;078O ?@54AB0B5;L=>9 65;57K. > =0G0;0 ;5G5=8O
=5>1E>48<> ?@>25AB8 @5:B0;L=>5 >1A;54>20=85 ?@54AB0B5;L=>9 65;57K 8 ?@8 =5>1E>48<>AB8
B5AB =0 >?@545;5=85 C@>2=O A?5F8D8G5A:>3> 0=B835=0 ?@54AB0B5;L=>9 65;57K (PSA) 4> =0G0;0
8 G5@57 >48=0:>2K5 ?@<<56CB:8 2@5<5=8 2> 2@5
07=0G0BL ;5:0@AB25==>5 A@54AB2> ?0F85=B0< A B065;>9 D>@<>9 ?>G5G=>9 =54>AB0B>G=>AB8
(;8@5=A :@50B8=8=0 <10<;<8=) =5>1E>48<> A >A>1>9 >AB>@>6=>ABLN, ?>A:>;L:C ;:8=8G5A:8E
8AA;54>20=89 ?> ?@85=5=8N ;5:0@AB25==>3> A@54AB20 B0:8< ?0F85=B0< =5 ?@>2>48;8.
=5:>B>@KE ?0F85=B>2, :>B>@K5 ?@8<5=O;8 B078=, 2> 2@53> 2<5H0B5;LAB20 ?> ?>2>4C
:0B0@0:BK 8 3;0C:>B<5G0;AO A8=4@<< 0B>=8G5A:>3> 7@0G:0 (IFIS, 20@80=B A8=4@<<0
AC65==>3> 7@0G:0), GB> <>65B AB0BL ?@8G8=>9 C25;8G5=8O :;>8G5AB20 >A;>6=5=89 2> 2@5A;5
?@>2545=8O B0:>9 >?5@0F88.
0: ?@028;>, 70 1-2 =545;8 4> ?@>2545=8O >?5@0F88 ?> ?>2>4C :0B0@0:BK 8 3;0C:<<5=4C5BAO
?@5:@0B8BL ;5G5=85 B078=><, >4=0:> ?>;L70 >B ?@5:@015=8O ;5G5=8O B078=>< =0 A53>4=OH=89
45=L B>G=>=5 CAB0=>2;5=0. !>>1I0;>AL B0:65 > A8=4@<<5 0B>=8G5A:>3> 7@0G:0 A>>1I0;>AL
B0:65 C ?0F85=B>2, :>B>@K5 ?@5:@0B8;8 ?@8<5=5=85 B078=0 704>;3> 4> ?@>2545=8O
>?5@0B82=>3> 2<5H0B5;LAB20 ?> ?>2>4C :0B0@0:BK.
0F85=B0< ?5@54 ?;0=>2>9 >?5@0F859 ?> ?>2>4C :0B0@0:BK 8;8 3;0C:<<5=4C5BAO =0G8=0BL ?@8
<5=5=85 B078=0 384@>E;>@840. @8 ?>43>B>2:5 :>?5@0F88 E8@C@38 8 >DB0;L<>;>38 4>;6=K
C7=0BL, ?@8<5=O ;8 (8;8 ?@8<5=O5B) ?0F85=B B078=, A F5;LN ?@54C?@5645=8O 2>7<>6=KE
>A;>6=5=89, A2O70==KE AIFIS.
"078=0 384@>E;>@84 =5 A;54C5B =07=0G0BL 2 :<18=0F88 A A8;L=K<8 8=3818B>@0<8 CYP3A4
?0F85=B0< A =87:8< <5B01>;87<<< CYP2D6.
"078=0 384@>E;>@84 A;54C5B ?@8<5=OBL A >AB>@>6=>ABLN 2 :<18=0F88 A A8;L=K<8 8 C
<5@5==K<8 8=3818B>@0<8 CYP3A4 (A@0745; «□708<>459AB285 A 4@C38<8 ;5:0@AB25==K<8
A@54AB20<8 8 4@C385 284K 2708<>459AB289»)).
725AB=K A;CG08 0;;5@38G5A:8E @50:F89 =0 B078= C ?0F85=B>2 A =0;8G85< 2 0=0<=575 0;;5@388 =0
AC;LD0=8;0<84K. !;54C5B A>1;N40BL >AB>@>6=>ABL ?@8 ?@8<5=5=88 B078=0 384@>E;>@840
?0F85=B0<, C :>B>@KE @0=55 >B<5G0;0AL 0;;5@380 =0 AC;LD0=8;0<84K.
@8<5=5=85 2 ?5@8>4 15@5<5==>AB8 8;8 :>@<;5=8O 3@C4LN.
45=>@< =5 ?>:070= 4;O ?@8<5=5=8O 65=18=0
\$5@B8;L=>ABL
<5NI85AO 40==K5 A2845B5;LAB2CNB, GB> 2> 2@578=0 =01;N40;8AL A;CG08 =0@CH5=8O
MO:C;OF88, @5B@>3@04=>9 MO:C;OF88 8 =54>AB0B>G=>9 MO:C;OF88.
!>>A>I=>ABL 2;8OBL =0 A:>@>ABL @50:F88 ?@8 C?@02;5=88 02B>B@0=A?>@B>< 8;8 4@C38<8
<5E0=87<0<8.

AA;54>20=8O 2;8O=8O ?@5?0@0B0 =0 A?>A>1=>ABL C?@02;OBL 02B>B@0=A?>@B< 8;8 <5E0=87<0
<8 =5 ?@>2>48;8AL. 4=0:> ?0F85=BK 4>;6=K 1KBL ?@54C?@5645=K > 2>7<>6=>AB8 2>7=8:=>25=8O
3>;>2>:@C65=8O.

!>A>1 ?@8<5=5=8O 8 4>7K.

5:<5=4>20==0O 4>7O 4;O 27@>A;KE 1 :0?AC;0 5654=52=>, ?>A;5 702B@0:0; :0?AC;C A;54C5B
3;>B0BL F5;>9 A <>;>:< 8;8 2>4>9 (?@81;878B5;L=> 150<);, AB>O 8;8 A84O; :0?AC;C ?@8=8<0BL
F5;>9, =5 @07652K20O, ?>A.>;L:C MB> 1C45B ?@5?OBAB2>20BL <>48D8F8@>20==>1>645=8N
0:B82=>3> 8=3@5485=B0.

5B8.

5:0@AB25==>5 A@54AB2> =5 ?@8<5=OBL 45BO
57>?0A=>ABL 8 MDD5:B82=>ABL ?@8<5=5=8O B078=0 4;O 45B59 (4> 18 ;5B) =5 >F5=820;0AL.

5@54>78@>2:0.

!8
5@54>78@>2:0 B078=0 384@>E;>@84<< <>65B 2K720BL BO65;>5 38?>B5=782=>5 459AB285. "O65;>5
38?>B5=782=>5 459AB285 >B<5G0;>AL ?@8 @07=KE AB5?5=OE ?5@54>78@>2:8.
5G5=85.

A;CG05 @57:>3> A=865=8O 402;5=8O 2A;54AB285 ?5@54>78@>2:8 A;54C5B ?@>2>48BL
?>445@6820NICN B5@0?8N, =0?@02;5==CN =0 2>AAB0=>2;5=85 =>@<0;L=>9 DC=:F88 A5@45G=>-
A>AC48AB>9 A8AB578=0 A 15;:0<8 ?;072545=85 35<>480;870 2@04 ;8 O2;O5BAO F5;5A>>1@07=K
! F5;LN ?@5:@0I5=8O 40;L=59H53> 2A0AK20=8O ;5:0@AB25==>3> A@54AB20 <>6=> 8A:CAAB25==>
2K720BL @2>BC. @8 ?5@54>78@>2:5 7=0G8B5;L=K< :>;8G5AB2<< ;5:0@AB25==>3> A@54AB20
?0F85=BC =5>1E>48<> ?@>: A ?@8<5=5=85< 0:B828@>20==>3> C3;O 8 =87:>>A<>B8G5A:8E
A;018B5;L=KE A@54AB2, B0:8E :0: AC;LD0B =0B@8O.

>1>G=K5 @50:F88.

!> AB>@>=K =5@2=>9 A8AB53>;>2>:@C65=85; 3>;>2=0O 1>;L; >1<>@>:.
!> AB>@>=K >@30=>2 7@5=8O: 70BC<0=820=85 7@5=8O, =0@CH5=85 7@5=8O.
!> AB>@>=K A5@45G=>-A>AC48AB>9 A8AB5>IC15=85 A5@4F5185=8O; >@B>AB0B8G5A:0O
38?>B5=78O.
5A?8@0B>@=>-<5480AB8=0;L=K5 @0AAB@>9AB20: @8=8B; =>A>2>5 :@>2>B5G5=85.
!> AB>@>=K 65;C4>G=>-.8H5G=>3> B@0:B0: 70?>@, 480@5O, B>H=>B0, @2>B0.
!> AB>@>=K :>68 8 A;878ABKE >I>;>G5: AK?L, 7C4, :@0?82=8F0; 0=38=>52@>B8G5A:89 >B5;;
A8=4@<< !B825=A0 - 6=>A>=0; @<=0O M@8B5<0, M:AD>;80B82=K9 45@<0B8B.
!> AB>@>=K ?>;>2>9 A8AB5 @0AAB@>9AB20 MO:C;OF88, 2;;NG0O @5B@>3@04=CN MO:C;OF8N 8
=54>AB0B>G=>ABL MO:C;OF88.
!185 @0AAB@>9AB20: 0AB5=8O.
?8A0=K A;CG08 8=B@0?5@0F8>==>9 =5AB018;L=>AB8 @04C6=>9 >1>;>G:8 3;070 (A8=4@<<
AC65==>3> 7@0G:0) ?@8 >?5@0F88 ?> ?>2>4C :0B0@0:BK 8 3;0C:>2, :>B>@K5 ?@8=8<0;8 B078= (A
15==>AB8 ?@8<5=5=8O»).
<<8<> 2KH5C:070==KE ?>1>G=KE @50:F89, A>>1I0;>AL > A;CG0OE D81@8;;OF88 ?@54A5@489, 0@8B
<88, B0E8:0@488 8 48A?=>M, G0AB>B0 2>7=8:=>25=8O :>B>@KE =5 <>65B 1KBL 4>AB>25@=>
CAB0=>2;5=0.

!@>: 3>4=>AB8. 3 3>40.

#A;>28O E@0=5=8O.

%@0=8BL 2 >@838=0;L=>9 C?0:>2:5 ?@8 B5□.
%@0=8BL 2 =54>ABC?=<< 4;O 45B59 <5AB5.

#?0:>2:0.

> 10 :0?AC; 2 1;8AB5@5; ?> 3 1;8AB5@0 2 ?0G:5.

0B53>@8O >B?CA:0. > @5F5?BC.

@>872>48B5;L. «852A:89 28B0<8==K9 702>4».

5AB>=0E>645=85 ?@>872>48B5;O 8 53> 04@5A <5AB0 >ACI5AB2;5=8O 45OB5;L=>AB8.
04073, #: @08=0, 3. 852, C;. >?K;>2A:0O, 38.

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