

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

>:070==O.

>;53H5==O 1>;N B0 7<5=H5==O 70?0;5==O @V7=>3> ABC?5=O ?@8 @V7=8E AB0=0E, 2;;NG0NG8:
?0B>;>3VN AC3;>1V2: @52<0B>W4=89 0@B@8B, 0=:V;>7CNG89 A?>=48;VB, >AB5>0@B@8B,
3>AB@V =0?048 ?>403@8;
3>AB@V <07>2>-A:5;5B=V 70E2>@N20==O, B0:V O: ?5@V0@B@8B (=0?@8::04, ?;5G>;>?0B:>289
?5@V0@B@8B), B5=48=VB, B5=4>203V=VB, 1C@A8B;
V=HV ?0B>;>3VG=V AB0=8, A?@8G8=5=V B@02<0<8, C B<<8, 1V;L C ?>?5@5:C, @>7BO3=5==O,
2828E8, >@B>?548G=V, AB<0B>;>3VG=V B0 V=HV =57=0G=V >?5@0B82=V 2B@CG0==O.

@>B8?>:070==O.

V?5@GCB;82VABL 4> 4VNG>W @5G>28=8 01> 4> 1C4L-O:>3> V=H>3> :>5=B0 ?@5?0@0BC.
>AB@0 28@07:0 H;C=:0 01> :8H5G=8:C; H;C=:>2>-.8H:>20 :@>2>B5G0 01> ?5@D>@0FVO,
30AB@>V=B5=AB8=0;L=0 :@>2>B5G0 01> ?5@D>@0FVO 2 0=0<=57V ?VA;O 70AB>AC20==O
=5AB5@>W4=8E ?@>B870?0;L=8E ?@5?0@0BV2 (), 3>AB@0 01> @5F8482CNG0 28@07:0 H;C=:0
01> :8H5G=8:C 2 0=0<=57V (420 01> 1V;LH5 >:@5<8E 5?V7>4V2 2AB0=>2;5=>W 28@07:8 01>
:@>2>B5GV 2 0=0<=57V).
8;>D5=0.; O: V V=HV , ?@>B8?>:070=89 ?0FVT=B0<, C O:8E C 2V4?>2V4L =0 70AB>AC20==O
0F5B8;A0;VF8;>2>W :8A;>B8 01> V=H8E 28=8:0NBL 0=3V>=52@>B8G=89 =01@O.; ?>;V?8 =>A0,
=0?048 1@>=EV0;L=>W 0AB<8, :@>?82O=:0, 3>AB@89 @8=VB B0 V=HV 0;5@3VG=V A8<8.
>@CH5==O 35<>?>57C =52V4<><3> ?>E>465==O.
?O@=0 :@>2>B5G0 01> :@>2>B5G0 V=H>3> B8?C.
0?0;L=V 70E2>@N20==O :8H5G=8:C (E2>@>10 @>=0 01> 28@07:>289 :>;VB).
5GV=:>20 =54>AB0B=VABL.
8@:>20 =54>AB0B=VABL.
8@065=0 A5@F520 =54>AB0B=VABL (NYHA III-IV).
0ABV9=0 A5@F520 =54>AB0B=VABL (NYHA II-IV).
□H5@>10 A5@FO C ?0FVT=V2, O:V <0NBL AB5=>:0@4VN, ?5@5=5A5=89 V=D0@:B:0@40.
0E2>@N20==O ?5@8D5@8G=8E 0@B5@V9.
?O@=V 70E2>@N20==O C ?0FVT=V2, O:V ?5@5=5A;8 V=AC;LB 01> <0NBL 5?V7>48
B@0=78B>@=8E VH5
V:C20==O ?5@V>?5@0FV9=>3> 1>;N ?@8 0>@B>.:>@>=0@=> 28:>@8AB0==O 0?0@0BC
HBCG=>3> :@>2>>1V3C).
V:C20==O ?VA;O>?5@0FV9=>3> 1>;N ?VA;O >?5@0FVW :>@>=0@=>3> HC=BC20==O (01>
70AB>AC20==O 0?0@0BC HBCG=>3> :@>2>>1V3C).

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

VBV9. @8 >4=>G0A=>AC20==V 48;>D5=0: <>65 ?V428IC20B8 :>=F5=B@0FVN ;VBVN C ?;072V. 5:>
<5=4CTBLAO ?5@52V@OB8 @V2=V ;VBVN C ?;072V.
83>:A8=. >=F5=B@0FVO 483>:A8=C C ?;072V <>65 ?V428IC20B8AO ?@8 >4=>G0A=>AC20==V 7
48;>D5=0:>5=4CTBLAO ?5@52V@OB8 @V2=V 483>:A8=C C ?;072V.
VC@5B8:8 B0 0=B83V?5@B5=782=V ?@5?0@0B8. /: V ?@8 70AB>AC20==V V=H8E , >4=>G0A=5
70AB>AC20==O 8;;0:C□ ID <>65 >A;01;N20B8 0=B83V?5@B5=782=C 4VN 4VC@5B8:V2 01>
0=B83V?5@B5=782=8E ?@5?0@0BV2 (=0?@8::04, 15B0-1;>:0B>@V2, V=3V1VB>@V2 0=3V>B5=78=
?5@5B2>@N20;L=>3> D5@<5=BC (\$) H;OE<< ?@83=VG5==O A8=B57C 207>48;0B0B>@=8E
?@>AB03;0=48=V2. "><1V=0FVN A;V4 70AB>A>2C20B8 7 >15@56=VABN; ?0FVT=B0<, >A>1;82>
>VB=L>3> 2V:C, A;V4 @53C;O@=> :>=B@>;N20B8 0@B5@V0;L=89 B8A.: 0FVT=B8 ?>28==V >B@86
A;V4 ?5@52V@OB8 DC=:FVN =8@>: =0 ?>G0B:C :><1V=>20=>W B5@0?VW, 0 =040;V @53C;O@=>;
7>:@5<0 G5@57 ?V428I5=89 @878: =5D@>B>:A8G=>ABV ?@8 70AB>AC20==V 4VC@5B8:V2 B0
V=3V1VB>@V2 \$.
=B8:>03C;O=B8 B0 0=B8B@><1>B8G=V 70A>18. 5:>5=4>20=> ?@87=0G0B8 7 >15@56=VABN,
>A:V;L:8 >4=>G0A=5 70AB>AC20==O <>65 ?V428IC20B8 @878: 28=8:=5==O :@>2>B5GV.

5:><5=4CTBLAO @5B5;L=89 =03;O4 70 ?0FVT=B0<8, O:V >4=>G0A=> 70AB>A>2CNBL 48:;>D5=0: V
0=B8:>03C;O=B8 V, C @07V =5>1EV4=>ABV, :>@5:FVO 4>7C20==O 0=B8:>03C;O=V2. /: V V=HV ,
48:;>D5=0: C 28A>:8E 4>70E <>65 >1>@>B=> ?@83=VGC20B8 03@530FVN B@><1>F8BV2.
=HV, C B>@8 F8:;>:A835=078-2 (&-2) V :>@B8:>AB5@>W48. 4=>G0A=5 70AB>AC20==O
48:;>D5=0:C B0 V=H8E A8AB5<=8E 01> :>@B8:>AB5@>W4V2 <>65 ?V428I8B8 @878: @>728B:C
H;C=:>2>-.8H:>2>W :@>2>B5GV 01> 28@07:8. !;V4 C=8:0B8 >4=>G0A=>3> 70AB>AC20==O 42>E 01>
1V;LH5 . 4=>G0A=5 70AB>AC20==O 48:;>D5=0:C B0 :>@B8:>AB5@>W4V2 <>65 ?V428I8B8 G0AB>BC
>1VG=8E @50:FV9.

@>B84V015B8G=V 70A>18. B@8<0=> >:@52V4><;5==O O: ?@> 3V?>3;V:5AC20==O 48:;>D5=0:C, I>
>B@51CT :>@83C20==O 4>78 ?@>B84V015B8G=8E 70A>1V2. FVTW ?@8G8=8 @5:><5=4CTBLAO
:>=B@>;N20B8 @V2=V 3;N:>78 C :@>2V O: 70AB5@56=89 70EV4 ?@>BO3<< :><1V=>20=>W
B5@0?VW.

@>15=5F84. V:0@AL:V 70A>18, I> 15=5F84, <>6CBL 28:;>8:0B8 70B@8D5=0:C.

5B>B@5:A0B. 8:;>D5=0: <>65 ?@83=VGC20B8 BC1C;O@=89 =8@:>289 ;;V@5=A <5B>B@5:A0BC, I>
?V428ICT @V25=L <5B>B@5:A0BC. !;V4 7 >15@56=VABN 70AB>A>2C20B8 , 2:;>NG0NG8 48:;>D5=0:;
?@8 ?@87=0G5==V <5=H =V6 70 24 3>48=8 ?5@54 ;V:C20==O< <5B>B@5:A0B<<, >A:V;L:8 @V2=V
<5B>B@5:A0BC C ?;072V V 9>3> B>:A8G=VABL<>6CBL 7@>AB0B8.

?>A?>@8=. 8:;>D5=0:, O: V V=HV , <>65 ?>A8;N20B8 =5D@>B>:A8G=VABL F8:;>A?>@8=C G5@57
2?;82 =0=8@:>2V ?@>AB03;0=48=8. # 72O7:C 7 F8< ?@5?0@0B A;V4 70AB>A>2C20B8 C 4>70E
=86G8E, =V6 4;O ?0FVT=V2, O:V =5 >B@8A?>@8=.

"0:@>;V >6;825 ?V428I5==O @878:C =5D@>B>:A8G=>ABV, O:I> ?@87=0G0B8 >4=>G0A=> 7 B0:@>;V
=B81V>B8:8 EV=>;=>2>3> @O4C. '5@57 270T<>4VN 0=B81V>B8:V2 EV=>;=>2>3> @O4C B0
<>6;820 ?>O20 AC4>

\$5=VB>W=. @8 >4=>G0A=>AC20==V D5=VB>W=C B0 48:;>D5=0:C A;V4 :>=B@>;N20B8
:>=F5=B@0FVN D5=VB>W=C C ?;072V, 2@0E>2CNG8 >GV:C20=5 71V;LH5==O 5:A?>78FVW
D5=VB>W=C.

>;5AB8?>; V E>;5AB8@0 0=V ?@5?0@0B8 <>6CBL 28:;>8:0B8 70B@8 7<5=H5==O 01A>@1FVW
48:;>D5=0:C. 2060NG8 =0 F5, @5:><5=4CTBLAO 70AB>A>2C20B8 48:;>D5=0: ?@8=09<=V 70 1 3>48=C
4> 01> G5@57 4-6 3>48= ?VA;O 22545==O :>;5AB8?>;C/E>;5AB8@0

!5@F52V 3;V:> 7848. 4=>G0A=5 70AB>AC20==O A5@F528E 3;V:>784V2 V ?0FVT=B0< <>65 A?@80B8
?>A8;5==N A5@F52>W =54>AB0B=>ABV, 7=865==N H284:>ABV ;;C1>G:>2>W DV;LB@0FVW V
?V428I5==N :>=F5=B@0FVW 3;V:>784C C ?;072V.

VD5?@8AB>=. =5 A;V4 70AB>A>2C20B8 ?@>BO3<< 8-12 4=V2 ?VA;O ?@89>=C, >A:V;L:8 <>6CBL 7
<5=H8B8 5D5:B =C.

>BC6=V CYP2C9 V=3V1VB>@8. 5:><5=4CTBLAO 7 >15@56=VABN ?@87=0G0B8 48:;>D5=0:
>4=>G0A=> 7 ?>BC6=8<8 V=3V1VB>@0<8 CYP2C9 (=0?@8:;04, AC;LDV=?V@07>=>< V 2>@8:>=07>;>
<), I> <>65 ?@8725AB8 4> 7=0G=>3> 71V;LH5==O <0:A8<0;L=>W :>=F5=B@0FVW C ?;072V B0
5:A?>78FVW 48:;>D5=0:C 70 @0EC=>: ?@83=VG5==O 9>3> <5B01>;V7

!5;5:B82=V V=3V1VB>@8 72>@>B=>3> 70E?>;5==O A5@>B>=V=C (!). !C?CB=T 70AB>AC20==O B0
!! <>65 71V;LHC20B8 @878: H;C=:>2>-.8H:>28E :@>2>B5G.

0A>18, 70AB>AC20==O O:8E <>65 A?@8G8=8B8 28=8: =5==O 3V?5@:0;VT!C?CB=T ;V:C20==O
:0;V9715@V30NG8<8 4VC@5B8:0<8, F8:;>A?>@8=><, B0:@>;V< 01> B@8<5B>?@8<< <>65 28:;>8:0B8
71V;LH5==O @V2=O A82>@>B:>2>3> :0;VN, O:89 A;V4 :>=B@>;N20B8.

A>1;82>ABV 70AB>AC20==O.

;O 7<5=H5==O @878:C 28=8: =5==O ?>1VG=8E @50:FV9 ;V:C20==O A;V4 @>?>G8=0B8 7 =09<5=H>W
5D5:B82=>W 4>78, O:C A;V4 ?@89<0B8 ?@>BO3<< =09:>@>BH>3> B5@=B@>;N A8
030;L=V. !;V4 C=8:0B8 >4=>G0A=>3> 70AB>AC20==O 48:;>D5=0:C B0 V=H8E A8AB5<=8E , 2:;>NG0NG8
A5;5:B82=V V=3V1VB>@8 &-2, G5@57 2V4ACB=VABL 1C4L O:8E 4>:07V2 A8=5@3VG=>3> 5D5:BC
B0 C 72O7:C 7 ?>B5=V9=8<8 048B82=8<8 ?>1VG=8<8 5D5:B0<8.

!;V4 7 >15@56=VABN ?@87=0G0B8 ;V:C20==O ?0FVT=B0< ;VB=L>3> 2V:C 2V4?>2V4=> 4> @5:>
<5=40FV9 4;O 40=>W 3@C?8 ?0FVT=V2. :>@5<0 @5:><5=4CTBLAO 70AB>AC20==O
0AB>AC20==O ;V:0@AL:8E D>@< 4;O ?5@>@0;L=>3> ?@89> D5=0: H284:>3> 282V;L=5==O, <>65
?V428IC20B8 H;C=:>2C =5?5@5=>A8

@8 70AB>AC20==V 48;:>D5=0:C, O: V V=H8E , @V4:><6CBL @>72820B8AO 0;5@3VG=V @50:FVW,
2;:NG0NG8 0=0DV;0:B8G=V/0=0DV;0:B>W4=V @50:FVW.
/: V V=HV , 48;:>D5=0: <65 <0A:C20B8 >7=0:8 V A8<8 V=D5:FVW.
@8 B@820;>@8AB0==V 0=0;35B8:V2 <6CBL 28=8:0B8 3;>2=V 1>;V. E =5<6=0 ;V:C20B8 ?V428I5=8
<8 4>70<8 48;:>D5=0:C.
6820==O 0;:>3>;N ?V4 G0A ?@89>D5=0:, <65 ?>A8;8B8 ?>1VG=V @50:FVW 7 1>;C H;C=:>2>-
:8H:>2>3> B@0:BC (" 01> F5=B@0;L=>W =5@2>2>W A8AB5<8 (&!).
A;V;L:8 8;:0 ID 7C, 9>3> =5 @5:><5=4CTBLAO ?@87=0G0B8 ?0FVT=B0< 7V A?04:>28<8 AB0=0<8, I->
AC?@>2>46CNBLAO =5?5@5=>A878, <0;L01A>@1FVTN 3;N:>78-30;0:B>78 B0 =54>AB0B=VABN
;0:B078.
!;V4 ?5@V>48G=> ?5@53;040B8 ?>B@518 ?0FVT=B0 C 70AB>AC20==V 48;:>D5=0:C 4;O ?>;53H5==O
A82V4L =0 B5@0?VN. >15@56=VABN 70AB>A>2C20B8 C ?0FVT=V2 AB0@H5 65 @>:V2.
?:82 =0 H;C=:>2>-.8H:>289 B@0:B. @8 70AB>AC20==V , 2;:NG0NG8 48;:>D5=0:, 2V47=0G0;8AO
H;C=:>2>-.8H:>20 :@>2>B5G0 (35<0B5<578A, <5;5=0), 28@07:0 01> ?5@D>@0FVO, I> <6CBL <0B8
;5B0;L=V =0A;V4:8. >=8 <6CBL 28=8:0B8 C 1C4L-O:89 ?5@V>4 G0AC 2?@>4>26 ;V:C20==O, 7 01> 157
A87=8E H;C=:>2>-.8H:>28E 70E2>@N20=L 2 0=0<=57V. # ?0FVT=V2 ;VB=L>3> 2V:C B0:V
CA;:04=5==O 70728G09 <0NBL 1V;LH A5@9>7=V =0A;V4:8. # @07V 28=8:5==O H;C=:>2>-.8H:>2>W
:@>2>B5GV 01> 28@07:8 40=89 ;V:0@AL:89 70AV1 A;V4 2V4
5B5;L=89 <548G=89 =03;04 V >A>1;820 >15@56=VABL ?>B@V1=V ?@8 ?@87=0G5==V 48;:>D5=0:C
?0FVT=B0< 7 A8<0<8, I> 2:07CNBL =0 ?>@CH5==O 7 1>;C (" 01> 7 ?V4>7@N20=>N 28@07:>N,
:@>2>B5G5N, ?5@D>@0FVTN H;C=:0 01> :8H5G=8:C 2 0=0<=57V. 878: 28=8:5==O F8E O28I
71V;LHCTBLAO 7 ?V428I5==O< 4>78 , 0 B0:>6 C ?0FVT=V2 7 28@07:>N 2 0=0<=57V, 7>:@5<0
CA;:04=5=>N :@>2>B5G5N 01> ?5@D>@0FVTN.
?0FVT=V2 ;VB=L>3> 2V:C A?>AB5@V30TBLAO ?V428I5=0 G0AB>B0 ?>1VG=8E @50:FV9 =0 ,
>A>1;82> H;C=:>2>-.8H:>20 :@>2>B5G0 B0 ?5@D>@0FVO, I> <6CBL <0B8 ;5B0;L=V =0A;V4:8.
;O 7=865==O @878:C 28=8:5==O ?>1VG=8E O28I 7 1>;C (" ;V:C20==O A;V4 @>7?>G8=0B8 7
=09=86G>W 5D5:B82=>W 4>78 B0 4>45@6C20B8AL WW.
!;V4 @>73;O=CB8 <6;82VABL :<1V=>20=>W B5@0?VW V7 70AB>AC20==O< 70E8A=8E 70A>1V2
(=0?@8;:04, ?@>AB>;C 01> V=3V1VB>@V2 ?@>B>=>W ?>6 C ?0FVT=V2, O:V ?>B@51CNBL
AC?CB=L>3> 70AB>AC20==O =87L:8E 4>7 0F5B8;A0;VF8;>2>W :8A;>B8/0A?V@8=C 01> V=H8E
;V:0@AL:8E 70A>1V2, I> <6CBL ?V428I5==O @878: ?>1VG=8E @50:FV9 7 1>;C (".
!;V4 4>B@815@56=>ABV ?@8 AC?CB=L>!! , 0=B803@530=B=V ?@5?0@0B8 (=0?@8;:04,
0F5B8;A0;VF8;>20 :8A;>B0).
?:82 =0 ?5GV=:C. 5B5;L=89 <548G=89 =03;04 ?>B@V15= C 28?04:C, O:I> ?@5?0@0B =5>1EV4=>
?@87=0G0B8 ?0FVT=B0< 7 ?>@CH5==O< DC=:FVW ?5GV=:8, >A:V;L:8 WE AB0=<65
703>AB@8B8AO.
@8 70AB>AC20==V , 2;:NG0NG8 48;:>D5=0:, @V25=L >4=>3> 01> 1V;LH5 ?5GV=:>28E D5@<5=V2
<65 ?V428I5==O B8AO. V4 G0A B@820;>3> ;V:C20==O 48;:>D5=0:< C O:>ABV 70?>1V6=>3> 70E>4C
?>:070=89 @53C;O@=89 :>=B@>;L DC=:FVW ?5GV=:8.
A>1;82> @5B5;L=89 =03;04 ?>B@V15= C 28?04:C ?>@CH5=L DC=:FVW ?5GV=:8 157?>A5@54=L>
?VA;O 25;8:8E EV@C@3VG=8E 2B@CG0=L C 7207:C 7 @878:< 28=8:5==O :@>2>B5GV.
/:I> 7:07=8:V2 DC=:FVW ?5GV=:8 715@V30TBLAO 01> ?>3V@HCTBLAO, 702;ONBLAO ;V=VG=V
>7=0:8 01> A8<8 70E2>@N20==O ?5GV=:8 01> A?>AB5@V30NBLAO V=HV ?@>O28 (5>78=>DV;VO,
28A8?8), 70AB>AC20==O ?@5?0@0BC A;V4 ?@8?8=8B8.
V4 G0A ?@89>D5=0:C <6;8289 @>728B>: 35?0B8BC 157 ?@>4@><0;L=8E A8
8;:0 ID A;V4 ?@87=0G0B8 BV;L:8 ?VA;O @5B5;L=>W >FV=:8 A?V22V4=>H5==O @878:C B0
:>@8ABV C 28?04:C 2@>465=>3> ?>@CH5==O <5B01>;V7@DV@8=C.
?:82 =0 =8@:8. A:V;L:8 ?V4 G0A 70AB>AC20==O A?>AB5@V30;0AO 70B@8A>1;82>W >15@56=>ABV
A;V4 4>B@870;VB8=>W @V48=8 7 1C4L-O:>W ?@8G8=8 (=0?@8;:04, 4> 01> ?VA;O
EV@C@3VG=>3> 2B@CG0==O). # B0:8E 28?04:0E ?@8 70AB>AC20==V 48;:>D5=0:C @5:>
<5=4CTBLAO ?@>2>48B8 <=>VB>@8=3 =8@:>2>W DC=:FVW C O:>ABV 70AB5@56=>3> 70E>4C.
VA;O ?@8?8=5==O B5@0?VW AB0= ?0FVT=V2, O: ?@028;>, =>@<0;V7CTBLAO.
030;>;, 728G=5 28:>@8AB0==O 0=0;35B8:V2, >A>1;82> C :><1V=0FVW 7 45;V;L:<0 7=51>;NNG8<8
?@5?0@0B0<8, <65 ?@8725AB8 4> B@820;>3> CH:>465==O =8@>: 7 @878:<< @>728B:C =8@:>2>W
=54>AB0B=>ABV (0=0;35B8G=0 =5D@>?0BVO).

?;82 =0 H:V@C. >2V4><;O;>AO ?@> A5@9>7=V @50:FVW 7 1>:C H:V@8 (45O:V 7 =8E<0;8 ;5B0;L=89 =0A;V4>:), C B>;V0B82=89 45@<0B8B, A8=4@< !BV25=A0-6>=A>=0 B0 B>:A8G=89 5?V45@<0;L=89 =5:@>;V7, O:V A?>AB5@V30;8AO 4C65 @V4:> ?V4 G0A 70AB>AC20==O 48;>D5=0:C. 0928189 @878: 28=8:=5==O F8E @50:FV9 VA=CT =0 ?>G0B:C B5@0?VW, 0 WE @>728B>: 2V47=0G0TBLAO C 1V;LH>ABV 28?04:V2 ?@>BO3< ?5@H>3> 1;82> @5B5;L=>3> =03;O4C ?>B@51CNBL ?0FVT=B8 7 0;5@3VG=8<8 @50:FVO<8 =0 V=HV @5G>28=8. !;V4 ?@8?8=8B8 ?@89< ?@5?0@0BC ?@8 ?5@H8E ?@>O20E 3V?5@GCB;82>ABV.

!8AB5<=89 G5@2>=89 2>2G0: B0 7@N20==O A?>;CG=>W B:0=8=8. # ?0FVT=BV2 V7 A8AB5<=8< G5@2>=8< 2>2G0:>< B0 7

0@4V>20A:C;O@=V B0 F5@51@>20A:C;O@=V ?@>O28. A=CT ?V42815=89 @878: B@<1>B8G=8E A5@F52>-AC48==8E B0 F5@51@>20A:C;O@=8E CA::04=5=L (2::;NG0NG8 V=D0@:B:0@40 B0 V=AC;LB) C 7207:C 7 ?@89><< , C B>D5=0:C, >A>1;82> ?@8 4>23>B@820;>:8<8 4>70<8.

V:C20==O 48;>D5=0:< 70728G09 =5 @5:><5=4CTBLAO ?0FVT=B0< 7 2AB0=>2;5=8<8 A5@F52>- AC48==8<8 70E2>@N20==O<8 (70ABV9=0 A5@F520 =54>AB0B=VABL, VH5@>10 A5@FO,

70E2>@N20==O ?5@8D5@8G=8E 0@B5@V9) 01> 7 =5:>=B@>;L>20=>N 0@B5@V0;L=>N 3V?5@B5=7VTN. "0:8< ?0FVT=B0< 0 B0:>6 E2>@8< 7V 7=0G=8<8 D0:B>@0<8 @878:C

:0@4V>20A:C;O@=8E O28I (=0?@8::04, 3V?5@B>=VO, 3V?5@;V?V45289 4V015B, :C@V==O) ?@87=0G0B8 48;>D5=0: <6=0 ;8H5 ?VA;O @5B5;L=>W ;V=VG=>W >FV=:8..

A:V;L:8 :0@4V>20A:C;O@=V @878:8 48;>D5=0:C <6CBL 7@>AB0B8 V7 71V;LH5==O< 4>78 B0 B@820;>ABV ;V:C20==O, 9>3> =5>1EV4=> 70AB>A>2C20B8 O:>>30 :>@>BH89 ?5@V>4 B0 C

=09=86GV9 5D5:B82=V9 4>7V. >7C ?@5?0@0BC A;V4 ?5@V>48G=> ?5@53;O40B8, >A>1;82> O:I> ;V:C20==O B@820T 1V;LH5 4 B86=V2 .

0FVT=BV2 A;V4 V=D>@>7=0:8 V A8<8 A5@9>7=8E A5@F52>-AC48==8E B@<1>B8G=8E CA::04=5=L (=0?@8::04, 1V;L C 3@C4OE, 7048H:0, A;01:VABL, ?>@CH5==O<>28), O:V <6CBL 28=8:=CB8

@0?B>2>. # @07V ?>O28 B0:8E A8 725@=CB8AO 4> ;V:0@O.

V4?>2V4=>3> <548G=>3> =03;O4C B0 :>=AC;LBC20==O ?>B@51CNBL ?0FVT=B8 7 3V?5@B5=7VTN B0/01> 70ABV9=>N A5@F52>N =54>AB0B=VABN ;53:>3> 01> ?>3> ABC?5=O 2 0=0<=57V, >A:V;L:8 ?V4

G0A 70AB>AC20==O A?>AB5@V30;0AO 70B@8

5<0B>;>3VG=V ?@>O28. V4 G0A B@820;>3> ;V:C20==O 48;>D5=0:< @5:><5=4CTBLAO

:>=B@>;N20B8 ?>:07=8:8 :@>2V 7 287=0G5==O< :V;L:>ABV D>@<5=8E 5;5<5=BV2. 8;>D5=0: <65 >1>@>B=> ?@83=VGC20B8 03@530FVN B@<1>F8BV2. 0FVT=B8 7 ?>@CH5==O<8 35<>AB07C, 35 <>@03VG=8< 4V0B57>< 01> 35<0B>;>3VG=8<8 2V4E8;5==O<8 ?>B@51CNBL @5B5;L=>3> =03;O4C.

5A?V@0B>@=V ?@>O28. # ?0FVT=BV2 7 0AB<>N, A57>==8< 0;5@3VG=8< @8=VB><, =01@O:>< =070;L=>W A;87>2>W >1>;>=:8 (=0?@8::04, =070;L=8<8 ?>V?0<8), E@>=VG=8<8 >1AB@C:B82=8<8

70E2>@N20==O<8 ;535=V2 01> E@>=VG=8<8 V=D5:FVO<8 @5A?V@0B>@=>3> B@0:BC (>A>1;82> ?@8 =0O2=>ABV 7207:C 7 A8<0<8, ?>4V1=8<8 4> 0;5@3VG=>3> @8=VBC), @50:FVW =0, ?>4V1=V 4>

703>AB@5=L 0AB<8 (B0: 720=0 0A?V@8=>20 0AB<0 7 =5?5@5=>A8?82O=:0 7CAB@VG0NBLAO G0ABVH5, =V6 C V=H8E ?0FVT=BV2. # 7207:C 7 F8< B0:8< ?0FVT=B0< @5:><5=4CNBLAO

A?5FV0;L=V 70AB5@56=V 70E>48 (3>B>2=VABL 4> =040==O =52V4::04=>W 4>?>>38). &5 B0:>6 AB>ACTBLAO ?0FVT=BV2, C O:8E A?>AB5@V30NBLAO 0;5@3VG=V @50:FVW =0 V=HV @5G>28=8

7 1>:C H:V@8.

/: V V=HV 70A>18, I> ?@83=VGCNBL 0:B82=VABL ?@>AB03;0=48=A8=B5B078, 48;>D5=0:<65

28::8:0B8 1@>=E>A?07< C 28?04:C ?@87=0G5==O ?0FVT=B0< 7 0AB<>N (C B>

V=>G0 D5@B8;L=VABL. 40=V, I> 70AB>AC20==O<>65 =530B82=> 2?;820B8 =0 D5@B8;L=VABL 6V=>:, B>W 3@C?8 =5 @5:><5=4CTBLAO ?@87=0G0B8 6V=:0<, O:V ?;0=CNBL 203VB=VABL, 01> ?0FVT=B:0

<, O:V AB@0640NBL =0 157?;V44O.

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

?5@V>4 V B@8<5AB@V2 203VB=>ABV 8::0: ID <>6=0 ?@87=0G0B8 ;8H5 C B8E 28?04:0E, :>;8

>GV:C20=0 :>@8ABL 4;O<0B5@V ?5@528ICT ?>B5=FV9=89 @878: 4;O ?;>40, V ;8H5 2 < B@820;>ABV ;V:C20==O.

03VB=VABL. @83=VG5==O A8=B57C ?@>AB03;0=48=V2 <>65 =530B82=> ?>7=0G8B8AO =0
203VB=>ABV B0/01> 5<1@V>=0;L=>728B:C. 0=V 5?V45;>3VG=8E 4>A;V465=L A2V4G0BL ?@>
?V428I5=89 @878: 28:84=O B0/01> A5@F528E 204 V 30AB@>H878AC ?VA;O 70AB>AC20==O
V=3V1VB>@V2 A8=B57C ?@>AB03;0=48=V2 C @0==V B5@ABV. 2060TBLAO, I> @878:
?V428ICTBLAO ?@8 71V;LH5==V 4>78 V B@820;>ABV B5@0?VW.
V4 G0A B@8<5AB@C 203VB=>ABV 2AV V=3V1VB>@8 A8=B57C ?@>AB03;0=48=V2<>6CBL 2?;820B8
=0 ?;V4 =0ABC?=8< G8=>
A5@F52>;535=520 B>:A8G=VABL (7 ?5@54G0A=8< 70:@8BBO< 0@B5@V0;L=>W ?@>B>:8 B0
;535=52>N 3V?5@B5=7VTN);
?>@CH5==O DC=:FVW =8@>.: I> <>65 ?@>3@5AC20B8 4> =8@>:2>W =54>AB0B=>ABV 7
>;V3>3V4@>0<=V>7>
0?@8:V=FV 203VB=>ABV <>6CBL 28=8:0B8 =0ABC?=V O28I0:
<>6;825 ?>4>265==O G0AC :@>2>B5GV, 0=B803@530=B=89 5D5:B <>65 A?>AB5@V30B8AO =02VBL
?@8 4C65 =87L:8E 4>70E;
30;L@>G5=L <0B:8, I> ?@872>48BL 4> 70B@8 ?>4>265==O ?>;>3V2.
B65, 8;:0 ID ?@>B8?>:070=89 C B@8<5AB@V 203VB=>ABV.
>4C20==O 3@C44N
/: V V=HV , 48;:>D5=0: C =525;8:8E :V;L:>ABOE ?@>=8:0T C 3@C4=5<>;>:, B>B8?>:070=89 C ?5@V>4
3>4C20==O 3@C44N.

V=>G0 D5@B8;L=VABL

/: V V=HV , 48;:>D5=0: <>65 2?;820B8 =0 6V=>GC D5@B8;L=VABL V B<5=4>20=89 6V=:0<, O:V
?;0=CNBL 203VB=VABL. !;V4 @>73;O=CB8 ?8B0==O ?@> ?@8?8=5==O 70AB>AC20==O 48;:>D5=0:C
6V=:0<, O:V =5 <>6CBL 70203VB=VB8, 0 B0:>6 6V=:0<, O:8< ?@>2>48BLAO >1AB565==O AB>A>2=>
157?;V4=>ABV.

**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.**

0FVT=B0<, C O:8E ?V4 G0A ?@89>

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

>7C ?@5?0@0BC ?V418@0NBL V=482V4C0;L=>, ?>G8=0NG8 7 A>2C20B8 =09<5=HC 5D5:B82=C 4>7C
?@>BO3<< =09:>@>BH>3> ?5@V>4C G0AC 4;O :>=B@>;N A82CNG8 70240==O ;V:C20==O C :>6=>3>
>:@5<>3> ?0FVT=B0.

5:><5=4>20=0 ?>G0B:>20 4>70 ?@5?0@0BC 4;O 4>@>A;8E AB0=>28BL 75-150<3 =0 4>1C 70;56=> 2V4
28@065=>ABV A8@N20==O. @8 B@820;V9 B5@0?VW, O: ?@028;>, 4>AB0B=V< T 70AB>AC20==O 1
B01;5B:8 (75 <3) =0 4>1C. /:I> A8<8 70E2>@N20==O =091V;LH 28@065=V ?@>BO3<< =>GV 01>
2@0=FV, 8;:0 ID A;V4 70AB>A>2C20B8 225G5@V.

0:A8<0;L=0 4>1>20 4>70 AB0=>28BL 150<3 V WW =5 A;V4 ?5@528IC20B8. 8;:0 ID ?@87=0G5=89 4;O
>@>B:>G0A=>3> 70AB>AC20==O (<0:A8
"@820;VABL ;V:C20==O 287=0G0T ;V:0@.

"01;5B:8 A;V4 :>2B0B8 FV;8<8, =5 @>76>2CNG8, 70?820NG8 4>AB0B=L>N :V;L:VABN @V48=8, 1060=>
?V4 G0A 01> ?VA;O W48.

VB8: 8;:0 ID =5 @5:><5=4>20=89 4;O 70AB>AC20==O 4VBO

0FVT=B8 ;VB=L>3> 2V:C: =5 2V47=0G0;>AO ;V=VG=> 7=0GCI8E 7

0FVT=B8 7 2AB0=>2;5=8<8 A5@F52>-AC48==8<8 70E2>@N20==O<8 B0 7=0G=8< @878:>< WE
28=8:=5==O. "0:8< ?0FVT=B0<, 0 B0:>6 E2>@8< 7 =5:>=B@>;L>20=>N 0@B5@V0;L=>N

3V?5@B5=7VTN ;V:C20==O 48;:>D5=0:< 70728G09 =5 @5:><5=4CTBLAO. # @07V =5>1EV4=>ABV
?@5?0@0B <>65 1CB8 ?@87=0G5=89 BV;L:8 ?VA;O @5B5;L=>W >FV=:8 A?V22V4=>H5==O @878:C V
>@8ABV C 4>7V ≤ 100<3 =0 4>1C V B@820;>ABV ;V:C20==O =5 1V;LH5 4 B86=V2.

0FVT=B8 7 ?>@CH5==O< DC=:FVW =8@>.: 8;:>D5=0: ?@>B8?>:070=89 ?@8 =8@>:2V9

=54>AB0B=>ABV. ;O ;V:C20==O ?0FVT=BV2 7 ?>@CH5==O< DC=:FVW =8@>: A;01:>3> 01> ?>3>
ABC?5=O ?@5?0@0B A;V4 70AB>A>2C20B8 7 >15@56=VABN.

0FVT=B8 7 ?>@CH5==O< DC=:FVW ?5GV=:8. 8;:>D5=0: ?@>B8?>:070=89 ?@8 ?5GV=:>2V9
=54>AB0B=>ABV. ;O ;V:C20==O ?0FVT=BV2 7 ?>@CH5==O< DC=:FVW ?5GV=:8 A;01:>3> 01> ?>3>
ABC?5=O ?@5?0@0B A;V4 70AB>A>2C20B8 7 >15@56=VABN.

VB8.
8;:0; ID ?@>B8?>:070=89 4;O ;V:C20==O 4VB59 G5@57 28A>:89 2W @5G>28=8 C B01;5BFV.

5@54>7C20==O.

5<0T B8?>2>W ;V=VG=>W :0@B8=8 ?5@54>7C20==O 48;:>D5=0:C. !8<0<8 ?5@54>7C20==O
48;:>D5=0:C <>6CBL 1CB8 3>;>2=89 1V;L, =C4>B0, 1V;L 2 5?V30AB@VW, 1;N20==O, H;C=:>2> -:8H:>20
:@>2>B5G0, 4V0@5O, 70?0<>@>G5==O, 457>@VT=B0FVO, :><0, A>=:82VABL, 71C465==O, HC< C
2CE0E, AC4><8. # 28?04:C 7=0G=>3> >B@CT==O <>6;82V 3>AB@0 =8@:>20 =54>AB0B=VABL V
?>H:>465==O ?5GV=:8.

V:C20==O 3>AB@>3> >B@CT==O ?>;O30T C 70AB>AC20==V 70E>4V2 ?V4B@8W V A8<0B8G=>W
B5@0?VW. !8<0B8G=V V ?V4B@848 ?>:070=V ?@8 B0:8E CA;:04=5==OE O: 0@B5@V0;L=0
3V?>B5=7VO, =8@:>20 =54>AB0B=VABL, AC4><=89 A8=4@<, ?>@CH5==O 7 1>:C (" V
?@83=VG5==O 48E0==O. 0;:>9<>2V@=>, I> B0:V A?5F8DVG=V ;V:C20;L=V 70E>48 O: D>@A>20=89
4VC@57, 4V0;V7 01> 35<>?5@DC7VO AB0=CBL :>@8A=8<8 4;O 282545==O , >A:V;L:8 0:B82=V
@5G>28=8 F8E ?@5?0@0BV2 7=0G=>N N 72O7CNBLAO 7 1V;:0<8 :@>2V V 707=0NBL V=B5=A82=>3>
<5B01>;V7B5=FV9=> B>:A8G=8E 4>7 <>6=0 70AB>AC20B8 0:B82>20=5 2C3V;;O, 0 ?VA;O ?@89>
B5=FV9=> =5157?5G=8E 4;O 68BBO 4>7 ?@>25AB8 H;C=:>2C 45;=>B0<820==O H;C=:0).

>1VG=V @50:FVW.

I>:C B@02=>3> B@0:BC: =C4>B0, 1;N20==O, 4V0@5O, 48A?5?AVO, 014>
I>:C =5@2>2>W A8AB5<8: 3>;>2=89 1V;L, 70?0<>@>G5==O, A>=:82VABL, ?V428I5=0 2B>
<;N20=VABL, ?0@5AB57VO, ?>3V@H5==O ?0<OBV, AC4><8, 2V4GCBBO B@82>38, B@5<>@,
?>@CH5==O A<0:C, ?>@CH5==O <>7:>2>3> :@>2>>1V3C, A?;CB0=VABL A2V4>>ABV,
30;NF8=0FVW, ?>@CH5==O GCB;82>ABV, 7030;L=5 =574C60==O, 0?>?;5:AVO.
A8EVG=V ?>@CH5==O: 457>@VT=B0FVO, 45?@5AVO, 157A>==O, =VG=V :>H<0@8,
4@0BV2;82VABL, ?A8E>B8G=V @>7;048.
I>:C A5@F52>-AC48==>W A8AB5<8: ?0;L?VB0FVO, 1V;L C 3@C4=V9 ;VBFV, A5@F520
=54>AB0B=VABL, V=D0@:B:0@40, 0@B5@V0;L=0 3V?5@B5=7VO, 3V?>B5=7VO, 20A:C;VB.
I>:C >@30=V2 7>@C: ?>@CH5==O 7>@C, =5GVB:VABL 7>@C, 48?;>?VO, =52@8B 7>@>2>3> =5@20.
I>:C >@30=V2 A;CEC: 25@B83>, 472V= C 2CE0E, ?>3V@H5==O A;CEC.
I>:C H:V@8 B0 ?V4H:V@=>W B:0=8=8: 70?0;L=V 7 28A8?8, :@>?82O=:0, 1C;L>7=89 28A8?, 5:75<0,
5@8B5<0, @<=0 5@8B5<0, A8=4@< !BV25=A0-6>=A>=0, B>:A8G=89 5?V45@<0;L=89 =5:@>;V7
(A8=4@< 09T;:0), 5:AD>;V0B82=89 45@<0B8B, 5@8B@>45@;>AAO, @50:FVW D>B>GCB;82>ABV,
?C@?C@0, 0;5@3VG=0 ?C@?C@0, A25@1V6.
I>:C =8@>: B0 A5G>282V4=8E H;OEV2: 3>AB@0 =8@:>20 =54>AB0B=VABL, 35<0BC@VO,
?@>B5W=C@VO, =5D@>B8G=89 A8=4@<, V=B5@AB8FV0;L=89 =5D@8B, ?0?V;O@=89 =5:@>7
=8@:8, 70B@8@30=V7
I>:C 35?0B>1V;V0@=>W A8AB5<8: ?V428I5==O 0:B82=>ABV B@0=A02BO=8FO, ?>@CH5==O
DC=:FVW ?5GV=:8, DC;L7 ?5GV=:8, ?5GV=:>20 =54>AB0B=VABL.
I>:C A8AB5<8 :@>2V B0 ;VW A8AB5<8: B@><1>F8B>?5=VO, ;59:>?5=VO, 0=5?5=VO, 03@0=C;>F8B>7.
5@H8<8 >7=0:0<8 @>7;04V2 7 1>:C :@>2V B0 ;VW A8AB5<8 <>6CBL 1CB8: ?V428I5==O B5@;V,
?>25@E=52V @0=8 C @>B>2V9 ?>@>6=8=V, 3@8?>?>4V1=V A8=8, 2B><0, =>A>2V :@>2>B5GV,
H:V@=V :@>2>28;828.
I>:C 48E0;L=>W A8AB5<8: 1@>=EV0;L=0 0AB<0 (2;:NG0NG8 48A?=>5), ?=52<>=VB.
I>:C VW A8AB5<8: @50:FVW 3V?5@GCB;82>ABV, 0=0DV;0:B8G=V B0 0=0DV;0:B>W4=V @50:FVW
(2;:NG0NG8 0@B5@V0;L=C 3V?>B5=7VN V H>:), 0=3V>=52@>B8G=89 =01@O: (2;:NG0NG8 =01@O:
>1;8GGO, O78:0, 3>@B0=V).
I>:C @5?@>4C:B82=>W A8AB5<8: VB5=FVO.
=D5:FV9=V 70E2>@N20==O: 703>AB@5==O 70?0;5=L, ?>2O70=8E 7 V=D5:FVO<8 (=0?@8;:04,
@>728B>: =5:@>B8G=>3> D0AF8BC), A8<8 0A5?B8G=>3> <5=V=3VBC.

0=V ;V=VG=8E 4>A;V465=L B0 5?V45;>3VG=V 40=V A2V4G0BL ?@> ?V428I5=89 @878: B@>
<1>B8G=8E CA:;04=5=L (=0?@8::04, V=D0@:B :0@40 G8 V=AC;LB), ?>2'O70=89 V7 70AB>AC20==O<
48:;>D5=0:C, 7>:@5<0 C 28A>:8E B5@0?52B8G=8E 4>70E (150 <3/4>1C) B0 ?@8 B@820;>AC20==V.

"5@ABV.3 @>:8.

#<>28 715@V30==O.

15@V30B8 ?@8 B5□.

15@V30B8 C =54>ABC?=>

#?0:>2:0.

> 10 B01;5B>: C 1;VAB5@V; ?> 2 (10□2) 01> 10 (10 □ 10) 1;VAB5@V2 C :0@B>==V9 :>@>1FV.

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

;O B01;5B>: ?> 75 <3:

8@>1=8:.

!0;NB0A \$0@<0 <1%, V<5GG8=0/Salutas Pharma GmbH, Germany.

VAF57=0E>465==O 28@>1=8:0 B0 9>3> 04@5A0 20465==O 4VO;L=>ABV.

BB>-2>=-N@V:5-;5T 1, 39179 0@;515=, V<5GG8=0/Otto-von-Guericke-Allee 1, 39179 Barleben, Germany.

;O B01;5B>: ?> 150 <3:

8@>1=8:8.

!0;NB0A \$0@<0 <1%, V<5GG8=0/Salutas Pharma GmbH, Germany

(28@>1=8FB2> in bulk, ?0:C20==O, 28?CA: A5@VW).

5: !. ., >;LI0/Lek S. A., Poland (?0:C20==O, 28?CA: A5@VW).

VAF57=0E>465==O 28@>1=8:V2 B0 WE 04@5A0 20465==O 4VO;L=>ABV.

BB>-2>=-N@V:5-;5T 1, 39179 0@;515=, V<5GG8=0/Otto-von-Guericke-Allee 1, 39179 Barleben, Germany.

50 !, 2C;. ><0=VT2AL:0, 02-672 0@H020, >;LI0/50 C, Domaniewska Str., 02-672 Warsaw, Poland.