

!" #&/
4;O <548G=>3> 70AB>AC20==O ?@5?0@0BC

"#!"®
(LANTUS"®)

!,:04:

4VNG0 @5G>28=0: V=AC;V=C 3;0@3V=;
1 <; @>7G8=C 4;O V=T:FV9 V=AC;V=C 3;0@3V=C;
1 :0@B@846
1 D;0:>=
4>?>28=8:
4;O @>7G8=C 4;O V=T:FV9 C :0@B@846V ?> 3 <;: F8=:C E;>@84, ;, 3;VF5@8= (85 %), :8A;>B0
E;>@8AB>2>4=520 :>=F5=B@>20=0, =0B@VN 3V4@>:A84, 2>40 4;O V='T:FV9.
4;O @>7G8=C 4;O V=T:FV9 C D;0:>=V ?> 10 <;:
F8=:C E;>@84, ;, ?>;VA>@10B 20, 3;VF5@8= (85 %), :8A;>B0 E;>@8AB>2>4=520 :>=F5=B@>20=0,
=0B@VN 3V4@>:A84, 2>40 4;O V='T:FV9.

V:0@AL:0 D>@<0. >7G8= 4;O V= T:FV9.

\$0@<0:>B5@0?52B8G=0 3@C?0. =AC;V=8 B0 0=0;>38 B@820;>W 4VW 4;O V= T:FV9.
>4 " 10 04.

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

>:070==O.

V:C20==O FC:@>2>3> 4V015BC C 4>@>A;8E, ?V4;VB:V2 B0 4VB59 2V:× 2V4 2 @>:V2.

@>B8?>:070==O.

V428I5=0 GCB;82VABL 4> 4VNG>W @5G>28=8 01> 4> 1C4L-O:>W 4>?>W @5G>28=8, I> 2E>48BL 4>
A;:04C ?@5?0@0BC.

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

>7C20==O

0=BCA® 3 V=AC;V=C B@820;>W 4VW. @5?0@0B 22>4OBL >48= @07 =0 45=L C 1C4L-O:89 G0A 4>18,
0;5 I>@07C 2 >48= V B>9 A0<89 G0A.
568< 4>7C20==O ?@5?0@0BC 0=BCA® (4>70 B0 G0A 22545==O) A;V4 ?V418@0B8 V=482V4C0;L=>.
0FVT=B0< E2>@8< =0 FC:@>289 4V015B -3> B8?C 0=BCA® B0:>6 <>6=0 70AB>A>2C20B8 >4=>G0A=>
7 ?5@>@0;L=8<8 ?@>B84V015B8G=8<8 ;V:0@AL:8<8 70A>10<8. !8;0 4VW FL>3> ;V:0@AL:>3> 70A>1C
28@060TBLAO 2 >48=8FOE. &V >48=8FV 70AB>A>2CNBLAO 28=OB:>2> 4;O ?@5?0@0BC 0=BCA® V
2V4@V7=ONBLAO 2V4 G8 >48=8FL, C O:8E 28@060TBLAO A8;0 4VW V=H8E 0=0;>3V2 V=AC;V=C
(482. @>74V; «\$0@<0:>;>3VG=V 2;0AB82>ABV»).

VB8 V ?V4;VB:8

57?5G=VABL V 5D5:B82=VABL V=AC;V=C 0=BCA® 1C;8 4>2545=V ?@8 9>3> 70AB>AC20==V C
?V4;VB:V2 B0 4VB59 2V:× 2V4 2 @>:V2 (482. @>74V; «\$0@<0:>;>3VG=V 2;0AB82>ABV»). 0=BCA®
=5 282G02AO C 4VB59 2V:× <>;>4H5 2 @>:V2.

0FVT=B8 ;VB=L>3> 2V:C 2V:>25 ?@>3@5ACNG5 ?>3V@H5==O DC=:FVW =8@>: <>65 AB0B8

?@8G8=>N ?>ABV9=>3> 7<5=H5==O ?>B@518 2 V=AC;V=V.

8@:>20 =54>AB0B=VABL
?0FVT=BV2 7 =8@:>2>N =54>AB0B=VABN ?>B@510 2 V=AC;V=V <>65 1CB8 7<5=H5=0 G5@57

?>A;01;5==O <5B01>;V7

5GV=:>20 =54>AB0B=VABL

?0FVT=BV2 7 ?5GV=:>2>N =54>AB0B=VABN ?>B@510 2 V=AC;V=V <>65 7<5=HC20B8AO G5@57
7=865==O 740B=>ABV 4> 3;N:>=5>35=57C B0 C?>2V;L=5==O <5B01>;V7

5@5EV4 2V4 V=H8E V=AC;V=V2 =0 ?@5?0@0B 0=BCA®

@8 ?5@5E>4V 2V4 AE5< ;V:C20==O V=AC;V=0<8 A5@54=L>W B@820;>ABV 4VW 01> B@820;>W 4VW =0 AE5< 0=BCA® <>65 28=8:=CB8 ?>B@510 C 778 1070;L=>3> V=AC;V=C, 0 B0:>6 C :>@5:FVW AC?CB=L>W ?@>B84V015B8G=>W B5@0?VW (4>7 V G0AC 22545==O 4>40B:>2> 70AB>A>20=8E 728G09=8E (@53C;O@) V=AC;V=V2 01> 0=0;>3V2 V=AC;V=C H284:>W 4VW G8 4>7 ?5@>@0;L=8E ?@>B84V015B8G=8E ;V:0@AL:8E 70A>1V2).

)>1 7<5=H8B8 @878: @>728B:C 3V?>3;V:5 C @0==V @0=:>2V 3>48=8, ?0FVT=B0<, O:V 7®, ?>B@V1=> 7<5=H8B8 4>7C 1070;L=>3> V=AC;V=C =0 20-30 % ?@>BO3< ?5@H8E B86=V2 ;V:C20==O.

#?@>4>26 FL>3> ?5@V>4C 7=865==O 4>78 <0T 1CB8, ?@8=09<=V G0AB:>2>, :>20=> 71V;LH5==O< 4>78 V=AC;V=C, 22545==O O:>3> ?>2'O70=5 V7 ?@89<0==O< W6V. VA;O 7025@H5==O FL>3> ?5@V>4C @568< 4>7C20==O A;V4 :>@83C20B8 V=482V4C0;L=>.

/: V ?@8 70AB>AC20==V V=H8E 0=0;>3V2 V=AC;V=C, C ?0FVT=BV2, O:V >B@878 V=AC;V=C 2=0A;V4>: =0O2=>ABV 0=B8BV; 4> ;N4AL:>3> V=AC;V=C, ?@8 ?5@5E>4V =0 0=BCA® <>65 A?>AB5@V30B8AO ?>:@0I0==O 2V4?>2V4V >@30=V7 V4 G0A ?5@5E>4C =0 V=H89 ?@5?0@0B B0 2?@>4>26 ?5@H8E B86=V2 ?VA;O FL>3> @5:> <5=4CTBLAO @5B5;L=> :>=B@>;N20B8 <5B01>;VG=V ?>:07=8:8.

>:@0I5==O <5B01>;VG=>3> :>=B@>;N V ?>2O70=5 7 F8< 71V;LH5==O GCB;82>ABV 4> V=AC;V=C <>6CBL ?>B@51C20B8 4>40B:>2>W :>@5:FVW @5687C20==O. >@5:FVO 4>78 B0:>6 <>65 7=04>18B8AO, =0?@8::04, ?@8 73> A?>A>1C 68BBO, 718, :>;8 74V9A=NTBLAO 22545==O V=AC;V=C, 01> ?@8 28=8:=5==V V=H8E D0:B>@V2, O:V A?@8ONBL ?V428I5==N AE8;L=>ABV 4> @>728B:C 3V?>- 01> 3V?5@3;V:574V; «A>1;82>ABV 70AB>AC20==O»).

! ?>AV1 22545==O 0=BCA® A;V4 22>48B8 ?V4H:V@=>.

0=BCA® =5 <>6=0 22>48B8 2=CB@VH=L>25==>. "@820;0 4VO ?@5?0@0BC 0=BCA® 7C<>2;5=0 9>3> 22545==O< C ?V4H:V@=>-68@>2C B:0=8=C. =CB@VH=L>25==5 22545==O 728G09=>W ?V4H:V@=>W 4>78 <>65 ?@8725AB8 4> 28=8:=5==O BO6:>W 3V?>3;V:5 5<0T :;V=VG=> 7=0GCI>W @V7=8FV C @V2=OE V=AC;V=C 01> 3;N:>78 2 A8@>20BFV :@>2V ?VA;O 22545==O 0=BCA® 2 014>?>4V1=>3> <'O70 01> AB53=0. @8 :>6=V9 =0ABC?=V9 V=T:FVW ;C A;V4 I>@07C 7 0=BCA® =5 <>6=0 7 @>72545==V <>65 7DV;L 4VW ?@5?0@0BC C G0AV. @V FL>3>, 7 (?@8F-@CG:0 4;O V=AC;V=C 0@B@846V V=AC;V=C 0=BCA® ?@87=0G5=V 4;O 28:>@8AB0==O BV;L:8 C H?@8F-@CG:0E O?BV5=, ;V:!B0@, CB>?5= 24, "0:BV?5= 01> AllStar™. (?@8F-@CG:8 A;V4 28:>@8AB>2C20B8 73V4=> 7 @5:<5=40FVO<8, =040=8<8 28@>1=8:< V=T:FV9=>3> ?@8AB@>N. !;V4 GVB:> 4>B@81=8:0 I>4> 28:>@8AB0==O H?@8F-@CG:8 ?V4 G0A 70?@02:8 :0@B@8460, ?@8T4=0==O 3>;:8 B0 22545==O V=T:FVW V=AC;V=C. /:I> H?@8F-@CG:0 4;O 22545==O V=AC;V=C ?>H:>465=0 01> =5 ?@0FNT =0;56=8< G8=>< (G5@57 <5E0=VG=V 45D5:B8), WW A;V4 7=8I8B8, 0 70@8AB>2C20B8 =>2C H?@8F-@CG:C. # @07V =5A?@02=>ABV H?@8F-@CG:8 (482. V=AB@C:FVN 7 28:>@8AB0==O H?@8F-@CG:8) @>7G8= 7 :0@B@8460 <>6=0 =01@0B8 C H?@8F (I> ?V4E>48BL 4;O 22545==O V=AC;V=C :>=F5=B@0FVTN 100 >48=8FL/<;) B0 7@>18B8 V=T:FVN. 0@B@846 5@54 B8< O: 2AB028B8 :0@B@846 C H?@8F-@CG:C, 9>3> =5>1EV4=> 28B@8<0B8 2?@>4>26 1-2 3>48= ?@8 :V<=0B=V9 B53> 28:>@8AB0==O3> <>6=0 70AB>A>2C20B8 ;8H5 B>4V, :>;8 @>7G8= C =L> 7>@8<, 15710@2=8<, 157 2848<8E B25@48E G0AB>G>: B0 <0T B0:C 6 :>=A8AB5=FVN, O: 2>40. A:V;L:8 0=BCA® T @>7G8=><, 2V= =5 28<030T @5ACA?5=4C20==O ?5@54 70AB>AC20==O 5@54 V=T:FVTN A;V4 2840;8B8 7 :0@B@8460 2AV 1C;L10H:8 ?>2VB@O (482. V=AB@C:FVW 7 28:>@8AB0==O H?@8F-@CG:8). 5 4>72>;OTBLAO 7=>2C =0?>2=N20B8 ?>@>6=V :0@B@846V. 5@54 :>6=>N V=T:FVTN A;V4 ?5@52V@OB8 5B8:5B:C =0 V=AC;V=V, I>1 C=8:=CB8 ?>8;>2>3> 22545==O 7074V; «A>1;82V 70E>48 157?5:8»).

\$:0:>= 5@52V@8B8 D;0:>= ?5@54 9>3> 28:>@8AB0==O3> <>6=0 70AB>A>2C20B8 ;8H5 B>4V, :>;8 @>7G8= C =L>7>@8<, 15710@2=8<, 157 2848<8E B25@48E G0AB>G>: B0 <0T B0:C 6 :>=A8AB5=FVN, O: 2>40. A:V;L:8 0=BCA® T @>7G8=><, 2V= =5 28<030T @5ACA?5=4C20==O ?5@54 70AB>AC20==O

5@54 :>6=>N V=T:FVTN A;V4 ?5@52V@OB8 5B8:5B:C =0 V=AC;V=V, I>1 C=8:=CB8 ?×8;:>2>3> 22545==O 7074V; «A>1;82V 70E>48 157?5:8»).

>1VG=V @50:FVW.

V?>3;V:5, T =09G0ABVH>N ?>1VG=>N @50:FVTN, I> A?>AB5@V30TBLAO ?V4 G0A V=AC;V=>B5@0?VW. >=0 28=8:0T B>4V, :>;8 4>70 22545=>3> V=AC;V=C ?5@528ICT ?>B@51C C =L> "01;8G=89 ?5@5;V: ?>1VG=8E @50:FV9 51060=V @50:FVW, ?>2O70=V V7 70AB>AC20==O< ?@5?0@0BC, I> A?>AB5@V30;8AO ?V4 G0A ;:V=VG=8E 4>A;V465=L, =02>4OBLAO =86G5 70 :;0A0<8 >@30=V2 B0 A8AB5< C ?>@O4:C 7 <5=H5==O G0AB>B8 28=8:=5==O (4C65 G0AB> (≥ 1/10); G0AB> (≥ 1/100 - < 1/10); =5G0AB> (≥ 1/1 000 - < 1/100); @V4:> (≥ 1/10 000 - < 1/1 000); 4C65 @V4:> (< 1/10 000). # :>6=V9 7 F8E 3@C? ?>1VG=V @50:FVW =02545=V C ?>@O4:C 7<5=H5==O ABC?5=O WE A5@9>7=>ABV.

;0A >@30=V2 B0 A8AB5< MedDRA	C65 G0AB>	'0AB>	5G0AB>	V4:>	C65 @V4:>
>7;048 7 1>:C VW A8AB5<8				;5@3VG=V @50:FVW	
5B01>;VG=V B0 0;V <5=B0@=V @>7;048	V?>3;V:5				
>7;048 7 1>:C =5@2>2>W A8AB5<8					8A3527VO
>7;048 7 1>:C >@30=V2 7>@C				>@CH5==O 7>@C, @5B8=>?0BVO	
>7;048 7 1>:C H:V@8 B0 ?V4H:V@=8E B:0=8=		V?>3V?5@B@> DW?0B@> DVO			
>7;048 7 1>:C >?>@=>- @CE>2>W A8AB5<8 B0 A?>;CG=>W B:0=8=8					V0;3VO
>@CH5==O 7030;L=>3> AB0=C B0 @50:FVW C		50:FVW C		01@O:	

?8A >:@5<8E ?>1VG=8E @50:FV9 5B01>;VG=V B0 0;V<5=B0@=V @>7;048 "O6:V 5?V7>48 3V?>3;V:5A>1;82> O:I> 2>=8 28=8:0NBL =5>4=>@07>2>, <>6CBL AB0B8 ?@8G8=>N C@065==O =5@2>2>W A8AB5<8. "@820;0 01> BO6:0 3V?>3;V:5 # 1030BL>E ?0FVT=BV2 ?>O2V A8 A2V4G0BL ?@> =54>AB0B=T =04E>465==O 3;N:>78 4> B:0=8= 3>;>2=>3> <>7:C (=59@>3;V:>?5=VO), ?5@54CNBL >7=0:8 04@5=5@3VG=>W :>=B@@@53C;OFVW. /: ?@028;>, G8< 1V;LH5 B0 H284H5 7=86CTBLAO @V25=L FC:@C 2 :@>2V, B8< 1V;LH 28@065=8< T D5=><5= 04@5=5@3VG=>W :>=B@@@53C;OFVW B0 9>3> A8<8. >7;048 7 1>:C VW A8AB5<8

;5@3VG=V @50:FVW =5309=>3> B8?C =0 V=AC;V= 28=8:0NBL @V4>: . @>O20<8 B0:8E @50:FV9 =0
V=AC;V= (C B>28=8 <>6CBL 1CB8, =0?@8::04, 35=5@0;V7>20=V @50:FVW 7 1>:C H:V@8,
0=3V>=52@>B8G=89 =01@O:, 1@>=E>A?07<, 3V?>B5=7VO V H>:, O:V <>6CBL AB0=>28B8 703@>7C
4;O 68BBO E2>@>3>.
2545==O ?@5?0@0BV2 V=AC;V=C <>65 28::8:0B8 CB2>@5==O 0=B8BV; 4> =L>3>. V4 G0A
::V=VG=8E 28?@>1C20=L C 3@C? ?0FVT=BV2, O:V >B@8< B0 V=AC;V=<> 3;0@3V=<>, CB2>@5==O
0=B8BV;; I> ?5@5E@5A=> @503C20;8 7 ;N4AL:8< V=AC;V=<> B0 V=AC;V=<> 3;0@3V=<>,
A?>AB5@V30;>AO 7 >4=0:>2>N G0AB>B>N. # @V4:VA=8E 28?04:0E G5@57 =0O2=VABL 0=B8BV; 4>
V=AC;V=C <>65 28=8:0B8 ?>B@510 C :>@5:FVW 4>78, I>1 ?>?5@548B8 28=8:=5==O 3V?>- 01>
3V?5@3;V:5
>7;048 7 1>:C >@30=V2 7>@C
=0G=0 778 C :@>2V <>65 A?@8G8=8B8 B825 ?>@CH5==O 7>@C 2=0A;V4>: B82>W 7@C B0 V=45:AC
@5D@0:FVW :@8HB0;8:0.
878: ?@>3@5AC20==O 4V015B8G=>W @5B8=>?0BVW 7<5=HCTBLAO ?@8 4>AO3=5==V B@820;>W
=>@<0;V70FVW @V2=O 3;N:>78 C :@>2V. 4=0: V=B5=A8DV:0FVO V=AC;V=>B5@0?VW V7 @V7:8<
?>:@0I5==O< 3;V:53> :>=B@>;N <>65 AC?@>2>46C20B8AO B828< ?>3V@H5==O< ?5@51V3C
4V015B8G=>W @5B8=>?0BVW. # E2>@8E =0 ?@>;VD5@0B82=C @5B8=>?0BVN, >A>1;82> C B8E, O:8
< =5 ?@>2>48;0AO D>B>:>03C;OFVO, 5?V7>48 BO6:>W 3V?>3;V:52>W 2B@0B8 7>@C.
>7;048 7 1>:C H:V@8 B0 ?V4H:V@=8E B:0=8=
/: V ?@8 70AB>AC20==V 1C4L-O:8E V=H8E ?@5?0@0BV2 V=AC;V=C, C 2545==O V=T:FVW 2 <560E
>:@5<>W V=T:FV9=>W 4V;O=:8<>65 4>?><>3B8 7<5=H8B8 FV O28I0 01> ?>?5@548B8 WE ?>O2C.
>@CH5==O 7030;L=>3> AB0=C B0 @50:FVW C
> @50:FV9, I> 28=8:0NBL C G5@2>=V==O H:V@8, 1V;L, A25@1V6, :@>?82'O=:0, ?@8?CE;VABL 01>
70?0;5==O. V;LHVABL =5BO6:8E @50:FV9 =0 V=AC;V=, O:V 28=8:0NBL C
@V4:0 V=AC;V= <>65 ?@872>48B8 4> 70B@8@30=V7O28 =01@O:V2, >A>1;82> C 28?04:0E, :>;8
7024O:8 ?>A8;5==N V=B5=A82=>ABV V=AC;V=>B5@0?VW 240TBLAO ?>:@0I8B8 3;V:5=B@>;L, O:89
4> FL>3> =5 1C2 045:20B=8

VB8

030;<< ?@>DV;L 157?5:8 ?@5?0@0BC C 4VB59 B0 ?V4;VB:V2 (<>;>4H5 18 @>:V2) =5
2V4@V7=OTBLAO 2V4 9>3> ?@>DV;N 157?5:8 C 4>@>A;8E ?0FVT=BV2.
72VB0E ?@> ?>1VG=V @50:FVW, >B@8<0=8E ?V4 G0A ?>AB<0@:5B8=3>2>3> A?>AB5@565==O,
?>2V4><;O;>AO ?@> 2V4=>A=> G0ABVH5 28=8:=5==O @50:FV9 C 6 @50:FV9 7 1>:C H:V@8 (28A8?,
:@>?82O=:0) C 4VB59 B0 ?V4;VB:V2 (≤18 @>:V2), ?>@V2=O=> V7 4>@>A;8<8.
0=V ;;V=VG=8E 4>A;V465=L 7 157?5:8 70AB>AC20==O ?@5?0@0BC C 4VB59 2V:<< <>;>4H5 2 @>:V2
=0@07V 2V4ACB=V.
>2V4><;5==O ?@> ?V4>7@N20=V ?>1VG=V @50:FVW
>2V4><;5==O ?@> ?V4>7@N20=V ?>1VG=V @50:FVW ?VA;O AE20;5==O ;V:0@AL:>3> 70A>1C
4>72V;L=8<8 >@30=0<8 T 206;82>N ?@>F54C@>N. ?OT 74V9A=N20B8 ?>ABV9=89 <=>VB>@8=3
A?V22V4=>H5==O «:>@8ABL/@878:» 70AB>AC20==O FL>3> ;V:0@AL:>3> 70A>1C. 548G=8E
?@0FV2=8:V2 ?@>AOBL ?>2V4><;OB8 ?@> CAV ?V4>7@N20=V ?>1VG=V @50:FVW G5@57
=0FV>=0;L=V A8AB5<8 ?>2V4><;5=L.

5@54>7C20==O.

!8<8

5@54>7C20==O V=AC;V=C <>65 ?@8725AB8 4> BO6:>W, 0 V=>4V B@820;>W 3V?>3;V:5
V:C20==O

5BO6:V 28?04:8 3V?>3;V:5

V;LH BO6:V 5?V7>48 3V?>3;V:52>46CNBLAO :<<>N, AC4<0<8 01> =52@>;>3VG=8<8 ?>@CH5==O<8,
28<030NBL 2=CB@VH=L<'O7>2>3>/?V4H:V@=>3> 22545==O 3;N:03>=C 01> 2=CB@VH=L>25==>3>
22545==O :>=F5=B@>20=>3> @>7G8=C 3;N:>78. A:V;L:8 3V?>3;V:5

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

03VB=VABL. 5 VA=CT ;;V=VG=8E 40=8E, >B@8<0=8E C E>4V :>=B@>;L>20=8E ;;V=VG=8E

4>A;V465=L, AB>A>2=> 70AB>AC20==O V=C;V=C 3;0@3V=C C ?5@V>4 203VB=>ABV. 5G8A;5==V
40=V I>4> 70AB>AC20==O FL>3> ?@5?0@0BC 203VB=8< 6V=:0< (T 40=V ?@> 300-1000 28?04:V2
203VB=>ABV), >B@8<0=V ?V4 G0A ?>AB<0@:5B8=3>2>3> A?>AB5@565==O, 2:07CNBL=0 B5, I>
V=AC;V= 3;0@3V= =5 <0T H:V4;82>3> 2?;82C =0 ?5@51V3 203VB=>ABV, 0 B0:>6 =5 A?@8G8=OT 0=V
204 @>728B:C C ?;>40/=>2>=0@>465=>3>, 0=V B>:A8G=>3> 2?;82C =0 =L>3>. >A;V465==O =0
;01>@0B>@=8E B20@8=0E =5 28O28;8 >7=0: @5?@>4C:B82=>W B>:A8G=>ABV. @5?0@0B 0=BCA®
<>6=0 ?@87=0G0B8 C ?5@V>4 203VB=>ABV, O:I> C FL>B@510.
0FVT=B:0< 7 4V015B><, I> 28=8: 4> 203VB=>ABV, 01> 7 35AB0FV9=8< 4V015B>< C?@>4>26 CAL>3>
?5@V>4C 203VB=>ABV 4C65 206;82> ?V4B@8 7=86CTBLAO (71V;LHCTBLAO @878: 28=8:=5==O
3V?>3;V:5
>4C20==O 3@C44N. >:8 I> =52V4><>, G8 ?@>=8:0T V=AC;V= 3;0@3V= C 3@C4=5 <>;>:> C ;N459.
8=8:=5==O 1C4L-O:8E <5B01>;VG=8E 5D5:BV2, A?@8G8=5=8E ?@>=8:=5==O< V=AC;V=C 3;0@3V=C 2
>@30=V7< =>2>=0@>465=>3>/=5<>2;OB8 V7 3@C4=8< <>;>:×, =5 >GV:CTBLAO, >A:V;L:8 V=AC;V=
3;0@3V= T ?5?B84><, O:89 C H;C=:>2>-.8H:>2>7I5?;NTBLAO =0 0:8A;>B8. 4=0: 6V=:8 ?V4 G0A
3@C4=>3> 283>4>2C20==O <>6CBL ?>B@51C20B8 :>@5:FVW 4>78 ?@5?0@0BC B0 4VTB8.
5?@>4C:B82=0 DC=:FVO. >A;V465==O =0 ;01>@0B>@=8E B20@8=0E =5 28O28;8 157?>A5@54=L>3>
H:V4;82>3> 2?;82C =0 @5?@>4C:B82=C DC=:FVN.

VB8.

57?5:0 B0 5D5:B82=VABL ?@5?0@0BC 0=BCA® 2AB0=>2;5=0 C 4VB59 2V:> 2V4 2 @>:V2 V AB0@H5.
A>1;82>ABV 70AB>AC20==O.

0=BCA® =5 T ?@5?0@0B>< 281>@C 4;O ;V:C20==O 4V015B8G=>3> :5B>0F84>7C. 03> C B0:8E
28?04:0E @5:>5=4CTBLAO 2=CB@VH=L>25==5 22545==O 728G09=>3> (@53C;O@) V=AC;V=C.
/I> C @57C;LB0BV ;V:C20==O =5 240TBLAO 4>AO3B8 4>AB0B=L>3> :>=B@>;N @V2=O 3;N:>78 01>
A?>AB5@V30TBLAO B5=45=FVO 4> 71V;LH5==O 5?V7>4V2 3V?>- G8 3V?5@3;V:57C20==O
?@5?0@0BC, A;V4 ?5@52V@8B8, G8 4>B@8@89 ?@87=0G5=8E @568W B5E=V:8 V=T:FV9=>3>
22545==O, 0 B0:>6 >FV=8B8 V=HV 206;82V D0:B>@8, O:V 2?;820NBL =0 5D5:B82=VABL ;V:C20==O.
5@52545==O ?0FVT=B0 =0 V=H89 B8? 01> <0@:C V=AC;V=C <0T 2V41C20B8AO ?V4 @5B5;L=8<
<548G=8< =03;04>7C V=AC;V=C.

2545==O ?@5?0@0BV2 V=AC;V=C <>65 7C<>28B8 CB2>@5==O 0=B8BV; 4> =L>3>. # @V4:VA=8E
28?04:0E G5@57 =0O2=VABL 0=B8BV; 4> V=AC;V=C<>65 28=8:0B8 ?>B@510 C :>@5:FVW 4>78 4;O
?@>DV;0:B8:8 3V?>- 01> 3V?5@3;V:574V; <>1VG=V @50:FVW»).

V?>3;V:5

'0A, G5@57 O:89 @>72820TBLAO 3V?>3;V:5DV;N 4VW V=AC;V=V2, I> 70AB>A>2CNBLAO, V B>
1V;LH AB01V;L=>3> =04E>465==O 2>@30=V7< 1070;L=>3> V=AC;V=C ?@8 70AB>AC20==V
?@5?0@0BC 0=BCA® A;V4 >GV:C20B8<5=H>W V<>2V@=>ABV 28=8:=5==O 3V?>3;V:54V O: C
@0==V @0=:>2V 3>48=8 3V?>3;V:5

>B@8A>1;82>W >15@56=>ABV V ?>A8;5=> :>=B@>;N20B8 @V25=L 3;N:>78 C :@>2V =5>1EV4=> B8<
?0FVT=B0<, C O:8E =0?048 3V?>3;V:56 ?0FVT=B0< 7 ?@>;VD5@0B82=>N @5B8=>?0BVTN, >A>1;82>
B8< 7 =8E, O:8< =5 ?@>2>48;0AO D>B>:>03C;OFVO (@878: 28=8:=5==O B@0=78B>@=>W
?>AB3V?>3;V:5W A;V?>B8).

0FVT=B0< =5>1EV4=> 7=0B8 ?@> B5, I> 70 ?52=8E >1AB028= ?5@HV A8<8 @>728B:C 3V?>3;V:5

- C O:8E A?>AB5@V30TBLAO 7=0G=5 ?>:@0I0==O 3;V:53> :>=B@>;N,
- C O:8E 3V?>3;V:572820TBLAO ?>ABC?>2>,
- ;VB=L>3> 2V:C,
- O:V ?5@59H;8 7 V=AC;V=C B20@8==>3> ?>E>465==O =0 ;N4AL:89 V=AC;V=,
- 7 02B>=><=>N (2535B0B82=>N) =59@>?0BVTN,
- O:V E2>@VNBL =0 4V015B C?@>4>26 B@820;>3> ?5@V>4C G0AC,
- 7 ?A8EVG=8<8 @>7;040<8,
- O:V >4=>G0A=> >B@8

B0:8E A8BC0FVOE <>65 28=8:0B8 BO6:0 3V?>3;V:5 C =L>3> 7=8782AO @V25=L 3;N:>78 C :@>2V.
A:V;L:8 V=AC;V= 3;0@3V= ?@8 ?V4H:V@=>4>26 B@820;>3> ?5@V>4C G0AC, F5 <>65 ?@8725AB8 4>
B>3>, I> 4;O =>@<0;V70FVW 3;V:53> AB0=C 28<030B8<5BLAO 1V;LH5 G0AC.

/:I> C E2>@>3> A?>AB5@V30TBLAO =>@<0;L=89 G8 7=865=89 @V25=L 3;V:>78;L>20=>3> 35
<>3;>1V=C, F5 <>65 2:07C20B8 =0 28=8:=5==O C =L>3> ?5@V>48G=8E =54V03=>AB>20=8E (>A>1;82>
=VG=8E) 5?V7>4V2 3V?>3;V:5
;O 7<5=H5==O @878:C 28=8:=5==O 3V?>3;V:57C20==O ?@5?0@0BC V E0@GC20==O, ?@028;L=5
22545==O V=AC;V=C, 0 B0:>6 ?>V=D>@<>20=VABL E2>@>3> AB>A>2=> A8;V:5@V2, O:V
?V428ICNBL AE8;L=VABL 4> 28=8:=5==O 3V?>3;V:5
- 7
- ?V428I5==O GCB;82>ABV 4> V=AC;V=C (=0?@8::04, ?@8 CAC=5==V AB@5A>28E D0:B>@V2),
- =5728G=5, =04 B@820;5 DV78G=5 =020=B065==O,
- AC?CB=T 70E2>@N20==O (=0?@8::04, 1;N20==O, 4V0@50),
- =5@0FV>=0;L=5 E0@GC20==O,
- ?@>?CA: ?@89<0==O W6V,
- 26820==O 0;:>3>;N,
- 45O:V ?>@CH5==O 5=4>:@8==>W A8AB5<8 (=0?@8::04, 3V?>B8@5>7, =54>AB0B=VABL
045=>3V?>DV70 G8 :>@8 =04=8@:>28E 70;>7) C AB04VW 45:>
- >4=>G0A=5 70AB>AC20==O 45O:8E V=H8E ;V:0@AL:8E 70A>1V2.
!C?CB=V 70E2>@N20==O
002=VABL AC?CB=L>3> 70E2>@N20==O 28<030T ?>A8;5==O :>=B@>;N 70 <5B01>;VG=8<8 ?>:07=8:0
<8. # 1030BL>E 28?04:0E ?>:070=5 ?@>2545==O 0=0;V7C A5GV =0 ?@8ACB=VABL :5B>=>28E BV; B0
G0AB> 28=8:0T =5>1EV4=VABL C :>@5:FVW 4>78 V=AC;V=C. >B@510 2 V=AC;V=V =5@V4:><>65
7@>AB0B8. 0FVT=B8, E2>@V =0 4V015B 1 B8?C, ?>28==V ?@>4>26C20B8 @53C;O@=> A?>6820B8
E>G0 1 =525;8:C :V;L:VABL 2C3;52>4V2, =02VBL O:I> 2>=8 740B=V ?@89<0B8 ;8H5 =57=0G=C
:V;L:VABL W6V 01> 7>2AV=5 <>6CBL ?@89<0B8 W6C, 01> C =8E 28=8:0T 1;N20==O. <=V:>;8 =5
A;V4 ?@8?8=OB8 70AB>AC20==O V=AC;V=C ?>2=VABN.
(?@8F-@CG:8, ?@840B=V 4;O :0@B@846V2 0=BCA®
0@B@846V V=AC;V=C 0=BCA® A;V4 28:>@8AB>2C20B8 ;8H5 C =0ABC?=8E H?@8F-@CG:0E:
O?BV5=, ;V:!B0@, CB>?5= 24, "0:BV?5= 01> AllStarTM. E =5 <>6=0 70AB>A>2C20B8 C V=H8E H?@8F-
@CG:0E 1030B>@07>2>3> 28:>@8AB0==O, >A:V;L:8 B>G=VABL 4>7C20==O 1C;0 287=0G5=0 BV;L:8
4;O 2:070=8E H?@8F-@CG>:. 5 CAV 7 F8E H?@8F-@CG>:<>6CBL ?@>4020B8AO C 20HV9 :@0W=V.
><8;:>25 22545==O V=H>3> ?@5?0@0BC
04E>48;8 ?>2V4><;5==O ?@> ?><8;:>25 22545==O ?@5?0@0BV2, :>;8 702> 22>48;8 V=HV V=AC;V=8,
7>:@5<0 V=AC;V=8 :>@>B:>W 4VW. 5@54 :>6=>N V=T:FVTN A;V4 ?5@52V@OB8 5B8:5B:C =0
V=AC;V=V, I>1 C=8:=CB8 ?<8;:>2>3> 22545==O 70
><1V=0FVO ?@5?0@0BC 0=BCA® 7 ?V>3;VB07>=><
@> 28?04:8 A5@F52>W =54>AB0B=>ABV ?>2V4><;O;>AO ?@8 70AB>AC20==V ?V>3;VB07>=C C
?>T4=0==V 7 V=AC;V=<, >A>1;82> C ?0FVT=BV2, O:V <0;8 D0:B>@8 @878:C @>728B:C A5@F52>W
=54>AB0B=>ABV. &5 A;V4 2@0E>2C20B8 ?@8 @>73;04V <>6;82>ABV ?@>2545==O ;V:C20==O :>
<1V=0FVTN ?V>3;VB07>=C B0 ?@5?0@0BC 0=BCA®. @8 70AB>AC20==V FVTW :<1V=0FVW
?0FVT=B8 <0NBL 1CB8 ?V4 =03;04< G5@57 <>6;82VABL 28=8:=5==O >7=0: V A8W =54>AB0B=>ABV,
71V;LH5==O <0A8 BV;0 V =01@O:C. @8 1C4L-O:>3V@H5==V :0@4V>;>3VG=8E A8AC20==O
?V>3;VB07>=C =5>1EV4=> ?@8?8=8B8.

**40B=VABL 2?;820B8 =0 H284:VABL @50:FVW ?@8 :5@C20==V 02B>B@0=A?>@B< 01> @>1>BV 7
V=H8<8 <5E0=V7<0<8.**

40B=VABL ?0FVT=B0 4> :>=F5=B@0FVW C2038 B0 H284:VABL 9>3> @50:FVW<>6CBL
?>@CHC20B8AO 2=0A;V4>: 28=8:=5==O 3V?>3;V:5, =0?@8::04, C=0A;V4>: 7>@>28E @>7;04V2. &5
<>65 1CB8 =5157?5G=8< C B8E A8BC0FVOE, :>;8 FV O:>ABV T >A>1;82> 206;828<8 (=0?@8::04, ?V4
G0A :5@C20==O B@0=A?>@B=8<8 70A>10<8 01> @>1>B8 7 <5E0=V7<0<8).
0FVT=B0< =5>1EV4=> ?>@048B8 26820B8 =5>1EV4=8E 70?>1V6=8E 70E>4V2 7 <5B>N C=8:=5==O
3V?>3;V:5@B=8< 70A>1>A>1;82> 206;828< 4;O B8E ?0FVT=BV2, C O:8E ?5@HV >7=0:8 @>728B:C
3V?>3;V:5 28@065=8<8 01> 27030;V 2V4ACB=V, 0 B0:>6 4;O E2>@8E, C O:8E 3V?>3;V:5A8BL G0AB>.
!;V4 @5B5;L=> 72068B8, G8 20@B> AV40B8 70 :5@< 01> ?@0FN20B8 7 <5E0=V7<0<8 C B0:>

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

A=CT @O4 @5G>28=, O:V 2?:820NBL=0 <5B01>;V7< 3;N:>78, 0 >B65, WE 70AB>AC20==O <>65 28
<030B8 :>@5:FVW 4>78 V=AC;V=C 3;0@3V=C.
> @5G>28=, O:V <>6CBL ?>A8;N20B8 FC:@>7=86CNG89 5D5:B V=AC;V=C B0 71V;LHC20B8
AE8;L=VABL 4> 28=8:=5==O 3V?>3;V:5@0;L=V ?@>B84V015B8G=V ;V:0@AL:V 70A>18,
V=3V1VB>@8 0=3V>B5=78=?5@5B2>@NNG>3> D5@<5=BC (\$), 487>?V@0:A5B8=, V=3V1VB>@8
<=>0:A84078 (), ?5=B>:A8DV;V=, ?@>?>:A8D5=, A0;VF8;0B8 B0 AC;LD0=V;B81=V 70A>18.
> @5G>28=, O:V <>6CBL ?>A;01;N20B8 FC:@>7=86CNG89 5D5:B V=AC;V=C, =0;560BL
:>@B8:>AB5@>W48, 40=07>;, 4V07>:A84, A5G>3V==V 70A>18, 3;N:03>=, V7>=V0784, 5AB@>35=8 B0
?@>35AB>35=8, ?>EV4=V D5=>BV078=C, A<0B@>?V=, ?@5?0@0B8-A8 5?V=5D@8= (04@5=0;V=),
A0;L1CB0<;, B5@1CB0;V=), 3>@<=>8 I8B>?>4V1=>W 70;>78, 0B8?>2V 0=B8?A8E>B8G=V ;V:0@AL:V
70A>18 (=0?@8;;04, :;>70?V= B0 >;0=70?V=) B0 V=3V1VB>@8 ?@>B507.
5B0-1;>:0B>@8, :;>=V48=, A>;V ;VBVN 01> 0;>3>;L <>6CBL O: ?>A8;N20B8, B0: V ?>A;01;N20B8
FC:@>7=86CNG89 5D5:B V=AC;V=C. 5=B0W V=>4V =0AB0T 3V?5@3;V:5
@V< B>3>, ?V4 4VTN A8;VB8G=8E 70A>1V2, B0:8E O: 15B0-1;>:0B>@8, :;>=V48=, 3C0=5B848= B0
@575@?V=, >7=0:8 04@5=5@3VG=>W :>=B@@53C;OFVW <>6CBL A;01H0B8 01> 7>2AV< 7=8:0B8.

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

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

=AC;V= 3;0@3V= @>7@>1;5=89 O: 0=0;>3 V=AC;V=C ;N48=8, O:89 <0T =87L:C @>7G8==VABL C
=59B@0;L=>28IV. # ?@5?0@0BV 0=BCA® 2V= T ?>2=VABN @>7G8==8< 7024O:8 :8A;>28IC @>7G8=C
4;O V=T:FV9 (@4). VA;O 22545==O C ?V4H:V@=V B:0=8=8 :8A;89 @>7G8= =59B@0;V7CTBLAO, I>
?@872>48BL 4> 28=8:=5==O ?@5F8?VB0BV2, 7 O:8E ?>ABV9=> 282V;L=OTBLAO =525;8:0 :V;L:VABL
V=AC;V=C 3;0@3V=C, I> 70157?5GCT ?;02=89 (157 ?V:V2) B0 ?5@5410GC20=89 ?@>DV;L :@82>W
70;56=>ABV «:>=F5=B@0FVW-G0A», 0 B0:>6 1V;LH B@820;C 4VN ?@5?0@0BC.
=AC;V= 3;0@3V= <5B01>;V7CTBLAO 4> 2 0:B82=8E <5B01>;VBV2 M1 B0 M2 (482. @>74V; «\$0@
<0:>:V=5B8:0»).

2O7C20==O 7 V=AC;V=>28< @5F5?B>@>A;V465=L in vitro A2V4G0BL ?@> B5, I> 0DV==VABL
V=AC;V=C 3;0@3V=C B0 9>3> <5B01>;VBV2 M1 V M2 4> V=AC;V=>2>3> @5F5?B>@C ;N48=8
?>4V1=0 4> 0DV==>ABV ;N4AL:>3> V=AC;V=C.

2O7C20==O 7 @5F5?B>@>< \$ -1 (V=AC;V=>?>4V1=>3> D0:B>@C @>ABC 1): 0DV==VABL V=AC;V=C
3;0@3V=C 4> @5F5?B>@C \$ -1 ?@81;87=> C 5-8 @07V2 28I0 70 0DV==VABL ;N4AL:>3> V=AC;V=C
(0;5 ?@81;87=> C 70-80 @07V2 =86G0, =V6 0DV==VABL \$ -1 4> FL>3> @5F5?B>@C), C B>9 G0A O:
<5B01>;VB8 M1 V M2 72O7CNBLAO 7 @5F5?B>@>< \$ -1 7 0DV==VABN, 45I> =86G>N 70 0DV==VABL
;N4AL:>3> V=AC;V=C.

030;L=0 B5@0?52B8G=0 :>=F5=B@0FVO V=AC;V=C (V=AC;V=C 3;0@3V=C B0 9>3> <5B01>;VBV2), I>
287=0G0;0AO C ?0FVT=BV2 7 FC:@>28< 4V015B<< 1 B8?C, 1C;0 7=0G=> =86G>N 70 BC, O:0 1C;0 1
=5>1EV4=>N 4;O =0?V2<0:A8<0;L=>3> 72O7C20==O 7 @5F5?B>@>< \$ -1 B0 4;O =0ABC?=>W
0:B820FVW 35==>?@>;VD5@0B82=>3> <5E0=V7@>< \$ -1. =4>35==89 \$ -1 C DV7V>;>3VG=8E
:>=F5=B@0FVOE <>65 0:B82C20B8 35==>?@>;VD5@0B82=89 <5E0=V7<; ?@>B5 B5@0?52B8G=V
:>=F5=B@0FVW V=AC;V=C, O:V 28:>@8AB>2CNBLAO ?@8 V=AC;V=>B5@0?VW, 2 B< 0=BCA®,
7=0G=> =86GV 70 D0@<0:>;>3VG=V :>=F5=B@0FVW, =5>1EV4=V 4;O 0:B820FVW \$ -1-
>?>A5@54:>20=>3> <5E0=V7

09206;82VH>N 4VTN V=AC;V=C, C B>78. =AC;V= B0 9>3> 0=0;>38 7=86CNBL @V25=L 3;N:>78 2
:@>2V 70 @0EC=>: AB83> A?>6820==O ?5@8D5@8G=8<8 B:0=8=0<8, 7>:@5<0 A:5;5B=8<8 < O70<8 B0
68@>2>N B:0=8=>N, 0 B0:>6 ?@83=VG5==O CB2>@5==O 3;N:>78 C ?5GV=FV. =AC;V= ?@83=VGCT
;V?>;V7 2 048?>F8B0E B0 ?@>B5>;V7, >4=>G0A=> ?>A8;NNG8 A8=B57 1V;:0.

;V=V:>-D0@<0:>;>3VG=V 4>A;V465==O 4>25;8 5:2V20;5=B=VABL >4=0:>28E 4>7 V=AC;V=C
3;0@3V=C B0 V=AC;V=C ;N48=8 ?VA;O 2=CB@VH=L>25==>3> 22545==O F8E ?@5?0@0BV2. /: V ?@8
70AB>AC20==V 1C4L-O:8E V=AC;V=V2, =0 E0@0:B5@ 4VW V=AC;V=C 3;0@3V=C C G0AV<>6CBL
2?:820B8 DV78G=0 0:B82=VABL B0 V=HV G8==8:8.

>A;V465==O V7 70AB>AC20==O< <5B>4C DV:A0FVW 5C3;V:53> AB0=C, O:V ?@>2>48;8AO =0
74>@>28E >A>10E V E2>@8E =0 FC:@>289 4V015B B8?C, ?@>45<=>AB@C20;8, I>, =0 2V43> ?@>B0
@>0) V=AC;V=C ;N48=8, ?>G0B>: 4VW V=AC;V=C 3;0@3V=C ?VA;O ?V4H:V@=>3> 22545==O
=0AB0T ?V7=VH5, ?@5?0@0B 4VT ?;02=>, =5 28;;8:0NG8 ?>O28 ?V:V2 :>=F5=B@0FVW 3;N:>78 C
:@>2V, 0 B@820;VABL 9>3> 4VW ?@>;>=3>20=0.

57C;LB0B8 >4=>3> 7 4>A;V465=L A5@54 ?0FVT=BV2 =02545=V =0 3@0DV:C =86G5.

@>DV;L 0:B82=>ABV C E2>@8E =0 FC:@>289 4V015B B8?C

'0A (3>48=8), O:89 ?@>9H>2 ?VA;O ?V4H:V@=>W V=T:FVW

—————=AC;V= 3;0@3V= V=5FL ?5@V>4C A?>AB5@565==O

*- 28770G5=0 O: :V;L:VABL 3;N:>78, 22545=>W V=DC7%V=AC;V=O ?V4B@8ABV9=>3> @V2=O 3;N:>78 C ?;072V(I>3>48==V A5@54=V ?>:07=8:8).

V;LH0 B@820;VABL 4VW ?V4H:V@=> 22545=>3> V=AC;V=C 3;0@3V=C 157?>A5@54=L> ?>2O70=0 V7 ?>2V;L=VH>N 01A>@1FVTN, I> 4>72>;OT 70AB>A>2C20B8 ?@5?0@0B 1 @07 =0 4>1C. %0@0:B5@ 4VW C G0AV V=AC;V=C B0 9>3> 0=0;>3V2, B0:8E O: V=AC;V= 3;0@3V=, <65 <0B8 7=0G=C # >4=>1C20==V ?VA;O 2=CB@VH=L>25==>3> 22545==O V=AC;V=C 3;0@3V=C B0 V=AC;V=C ;N48=8 A8<8 3V?>3;V:5 :>=B@@53C;OFVW 3>@<=>0;L=>W 2V4?>2V4V 1C;8 0=0;>3VG=8<8 C 74>@>28E 4>1@>2>;LFV2 B0 E2>@8E =0 FC:@>289 4V015B 1 B8?C.

?;82 V=AC;V=C 3;0@3V=C (O:89 22>48;8 1 @07 =0 4>1C) =0 ?5@51V3 4V015B8G=>W @5B8=>?0BVW >FV=N202AO ?V4 G0A 2V4:@8B>3> ?OB8@VG=>3> 28?@>1C20==O, ?@5?0@0B< ?>@V2=O==O C O:>482AO 420 @078 =0 4>1C), I> ?@>2>48;>AO A5@54 1024 ?0FVT=BV2, E2>@8E =0 FC:@>289 4V015B B8?C, C O:8E A?>AB5@V30;>AO ?@>3@5AC20==O @5B8=>?0BVW =0 3 B0 1V;LH5 ?C=:B8 70 H:0;>N, I> 70AB>A>2C20;0AO C 4>A;V465==V « 0==T ;V:C20==O 4V015B8G=>W @5B8=>?0BVW» (Early Treatment Diabetic Retinopathy Study (ETDRS)). @>3@5AC20==O >FV=N20;>AO 70 4>?<>3>N D>B>3@0DC20==O >G=>3> 4=0. !B0B8AB8G=> 7=0GCI>W @V7=8FV 3@5AC20==O< 4V015B8G=>W @5B8=>?0BVW ?@8 22545==V V=AC;V=C 0=BCA® B0 % V=AC;V=C =5 1C;> 28O2;5=>.

>A;V465==O ORIGIN (Outcome Reduction with Initial Glargine INtervention, «=865==O @878:C =5A?@8OB;828E ;;V=VG=8E =0A;V4:V2 ?@8 ?5@28==> 1030B>F5=B@>28<, @0=4>20=8< 4>A;V465==O< 7 D0:B>@V0;L=8< 48709=>< 2x2, I> ?@>2>48;>AO 70 CG0ABN 12 537 ?0FVT=BV2 7 28A>:8< A5@F52>-AC48==8< (!) @878:<, C O:8E A?>AB5@V30;0AO ?>@CH5=0 3;V:5 ?>@CH5=0 B>;5@0=B=VABL 4> 3;N:>78 (") (12% CG0A=8:V2) G8 FC:@>289 4V015B 2 B8?C, 7 ?@82>4C O:>3> 2>=8 >B@8@0;L=89 ?@>B84V015B8G=89 ?@5?0@0B (88% CG0A=8:V2). #G0A=8:8 4>A;V465==O 1C;8 @0=4>20=V (1:1) 4;O >B@8<0==O 01> V=AC;V=C 3;0@3V=C (n=6264), 4>70 O:>3> B8B@C20;0AO 4> 4>AO3=5==O @V2=O 3;N:>78 2 ?;072V =0BI5 ≤95 <3/4; (5,3 <<>;L/;) 01> AB0=40@B=>W B5@0?VW (n =6273).

5@H8< ?>:07=8:< C A;;04V :<1V=>20=>W ?5@28==>W :V=F52>W B>G:8 1C2 G0A 4> ?5@H>3> =0AB0==O A<5@BV 7 !! ?@8G8=, =5D0B0;L=>3> V=D0@:BC :0@40 () 01> =5D0B0;L=>3> V=AC;LBC, 0 4@C38< ?>:07=8:< C A;;04V :<1V=>20=>W ?5@28==>W :V=F52>W B>G:8 1C2 G0A 4> ?5@H>3> =0AB0==O 1C4L-O:>W 7 F8E ?>4V9 :<1V=>20=>W ?5@28==>W :V=F52>W B>G:8 01> ?@>2545==O ?@>F54C@8 @520A:C;O@870FVW (:>@>=0@=8E, A>==8E 01> ?5@8D5@8G=8E AC48=) 01> 3>A?VB0;V70FVW 7 ?@82>4C A5@F52>W =54>AB0B=>ABV.

> 2B>@8==8E :V=F528E B>G>: =0;560;8 A<5@B=VABL 7 CAVE ?@8G8= V :<1V=>20=0 :V=F520 B>G:0 20A:C;O@=8E ?>4V9.

=AC;V= 3;0@3V= =5 7A=89 @878: !! 70E2>@N20=L V A<5@BV 7 !! ?@8G8= C ?>@V2=O==V 7V AB0=40@B=>N B5@0?VTN. 5 1C;> 2V4 @V7=8FV < 3;0@3V=>< V AB0=40@B=>N B5@0?VTN 70 >1> <0 ?>:07=8:0<8 C A;;04V :<1V=>20=>W ?5@28==>W :V=F52>W B>G:8; 70 6>4=>N A;;04>2>N :V=F52>W B>G:8, I> 2;;NG0T FV =5A?@8OB;82V ;;V=VG=V =0A;V4:8; 70 A<5@B=VABN 7 CAVE ?@8G8=; 01> 70 :<1V=>20=>N :V=F52>N B>G>N 20A:C;O@=8E ?>4V9.

!5@54=O 4>70 V=AC;V=C 3;0@3V=C C :V=FV 4>A;V465==O AB0=>28;0 0,42 4/:3. 0 ?>G0B:C 4>A;V465==O A5@54=V9 ?>:07=8: HbA1c 2 CG0A=8:V2 AB0=>282 6,4%, 0 =0 D>=V 4>A;V46C20=>3> ;V:C20==O ?>:07=8:8 HbA1c 20@VN20;8 2V4 5,9 4> 6,4% 2 3@C?V 70AB>AC20==O V=AC;V=C 3;0@3V=C V 2V4 6,2% 4> 6,6% 2 3@C?V 70AB>AC20==O AB0=40@B=>W B5@0?VW ?@>BO3< CAL>3> ?5@V>4C A?>AB5@565==O.

'0AB>B0 28=8:=5==O BO6:>W 3V?>3;V:5ABV CG0A=8:V2 4>A;V465==O, C O:8E A?>AB5@V30;8AO B0:V 5?V7>48, =0 100 ?0FVT=B>-@>:V2 ;V:C20==O) AB0=>28;0

1,05 2 3@C?V 70AB>AC20==O V=AC;V=C 3;0@3V=C V 0,30 2 3@C?V 70AB>AC20==O AB0=40@B=>W B5@0?VW, 0 G0AB>B0 ?V4B25@465=8E 5?V7>4V2 =5BO6:>W 3V?>3;V:528;0 7,71 2 3@C?V 70AB>AC20==O V=AC;V=C 3;0@3V=C V 2,44 2 3@C?V 70AB>AC20==O AB0=40@B=>W B5@0?VW. @>BO3>< FL>3> 6-@VG=>3> 4>A;V465==O C 42% ?0FVT=BV2 2 3@C?V 70AB>AC20==O V=AC;V=C 3;0@3V=C 27030;V =5 A?>AB5@V30;>AO 5?V7>4V2 3V?>3;V:5 0 >AB0==L>=0=>=V 4>A;V46C20=>3> ;V:C20==O, A?>AB5@V30;>AO ?V428I5==O <0A8 BV;0 2V4 28EV4=>3> @V2=O 2 3@C?V 70AB>AC20==O V=AC;V=C 3;0@3V=C 2 A5@54=L>AC20==O AB0=40@B=>W B5@0?VW.

VB8 B0 ?V4;VB:8

V4 G0A @0=4>20=>3> :>=B@>;L>20=>3> ;V=VG=>3> 4>A;V465==O 4VB8 (2V:< 2V4 6 4> 15 @>:V2), E2>@V =0 FC:@>289 4V015B 1 B8?C (n = 349), C?@>4>26 28 B86=V2 >B@8B5@0?VN C 1070;L=>- 1>;NA=>6=8< ?@89<0==O< W6V 22>482AO 728G09=89 ;N4AL:89 V=AC;V=. =AC;V= 3;0@3V= 22>48;8 1 @07 =0 =VG, 0 % V=AC;V= 22>48;8 1 01> 2 @078 =0 45=L. # >1>E 3@C?0E 2?;82 =0 @V25=L 3;V:>78;L>20=>3> 35<>3>;1V=C B0 G0AB>BC 28=8:=5==O 3V?>3;V:5 AC?@>2>46C20;0AO ;V=VG=8<8 ?@>O20<8, 1C2 0=0;>3VG=8<, ?@>B5 7=865==O @V2=O 3;N:>78 C ?;072V =0BI5A5@F5, ?>@V2=O=> 7 ?>G0B:>28< ?>:07=8:<, 1C;> 1V;LH8< C 3@C?V, O:0 >B@86 C 3@C?V, I> >B@828;0 2 @>:8. @8 ?@>4>265==V ;V:C20==O V=AC;V=< 3;0@3V=<< 6>4=8E =>28E A83=0;V2, O:V 1 A2V4G8;8 ?@> =5157?5:C, =5 1C;> >B@8<0=>.

"0:>6 1C;> ?@>2545=> ?5@5E@5A=5 ?>@V2=O;L=5 4>A;V465==O V=AC;V=C 3;0@3V=C ?;NA V=AC;V= ;V7?@> B0 % V=AC;V=C ?;NA 728G09=89 ;N4AL:89 V=AC;V= (:>65= 284 ;V:C20==O 70AB>A>2C202AO 2?@>4>26 16 B86=V2 28?04:>28< G8=><) C 26 ?V4;VB:V2, E2>@8E =0 4V015B 1 B8?C, 2V:< 2V4 12 4> 18 @>:V2. /: V C >?8A0=>A;V465==V A5@54 4VB59, 7=865==O @V2=O 3;N:>78 C :@>2V =0BI5A5@F5, ?>@V2=O=> 7 ?>G0B:>28< @V2=5<, 1C;> 28I5 C 3@C?V, I> >B@8@V2=O=> 7 ?>G0B:>28< @V2=5< 1C;8 0=0;>3VG=8<8 2 >1>E 3@C?0E, ?@>B5 =VG=V 3;V:5:07=8:8 1C;8 AB0B8AB8G=> 7=0GCI> 28I8<8 C 3@C?V, I> >B@8 =V6 C 3@C?V % V=AC;V=/728G09=89 V=AC;V=, ?@8 FL>:07=8:8 AB0=>28;8 5,4<B0 4,1 <. V4?>2V4=> V G0AB>B0 28=8:=5==O =VG=>W 3V?>3;V:528;0 32% C 3@C?V, I> >B@8, B0 52% C 3@C?V % V=AC;V=/728G09=89 V=AC;V=. C;> ?@>2545=> 24-B86=525 4>A;V465==O C ?0@0;5;L=8E 3@C?0E, 2 O:>28< 4V015B< 1 B8?C 2V:< 2V4 2 4> 6 @>:V2, 45 V=AC;V= 3;0@3V=, I> ?@87=0G02AO >48= @07 =0 4>1C 2@0=FW, ?>@V2=N202AO V7 %-V=AC;V=<<, I> ?@87=0G02AO >48= 01> 420 @078 =0 4>1C C O:>ABV 1070;L=>3> V=AC;V=C. #G0A=8:8 >1>E 3@C? 4>A;V465==O >B@8;NA=V V=T:FVW V=AC;V=C ?5@54 ?@89><< W6V.

>;>2=0 <5B0 4>A;V465==O ?@>45<=>AB@C20B8, I> % V=AC;V= ?@8=09<=V =5 <0T ?5@5203 ?5@54 V=AC;V=<< 3;0@3V=<< AB>A>2=> AC:C?=>3> @878:C 3V?>3;V:5AO3=CB0 =5 1C;0, V =0 D>=V 70AB>AC20==O V=AC;V=C 3;0@3V=C A?>AB5@V30;0AO B5=45=FVO 4> 71V;LH5==O G0AB>B8 3V?>3;V:54V9 [A?V22V4=>H5==O G0AB>B8 2 3@C?0E 70AB>AC20==O V=AC;V=C 3;0@3V=C: % (95%) = 1,18 (0,97-1,44)].

:07=8:V2 @V2=V2 3;V:>78;L>20=>3> 35<>3>;1V=C B0 3;N:>78 2 :@>2V 2 >1>E 4>A;V46C20=8E 3@C?0E 1C;0 ?>4V1=>N. >4=8E =>28E 40=8E I>4> 157?5G=>ABV 4>A;V46C20=8E ?@5?0@0BV2 C FL> A;V465==V =5 A?>AB5@V30;>AO.

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

>@V2=O==O :>=F5=B@0FVW V=AC;V=C 2 A8@>20BFV :@>2V C 74>@>28E >AV1 B0 C E2>@8E =0 FC:@>289 4V015B 2:07C20;> =0 1V;LH ?>2V;L=C B0 B@820;VHC 01A>@1FVN, 0 B0:>6 ?@>45 <=>AB@C20;> 2V4ACB=VABL ?V:C :>=F5=B@0FVW ?VA;O ?V4H:V@=>W V=T:FVW V=AC;V=C 3;0@3V=C ?>@V2=O=> 7 % V=AC;V=<< ;N48=8. "0:8< G8=><, >B@8<0=V :>=F5=B@0FVW V=AC;V=C 3;0@3V=C ?>2=VABN 2V4?>2V40;8 ?@>DV;N D0@<0:>48=0W 0:B82=>ABV ?@5?0@0BC C G0AV. 0 3@0DV:C, =02545=>45<=>AB@>20=89 ?@>DV;L 0:B82=>ABV V=AC;V=C 3;0@3V=C B0 % V=AC;V=C C G0AV.

@8 22545==V V=AC;V=C 3;0@3V=C 1 @07 =0 4>1C @V2=>206=0 :>=F5=B@0FVO 4>AO30TBLAO 265 G5@57

2-4 4=V ?VA;O ?5@H>W V=T:FVW.

@8 2=CB@VH=L>25==>48 =0?V2282545==O V=AC;V=C 3;0@3V=C B0 V=AC;V=C ;N48=8 1C;8 ?>@V2=N20=8<8.

VA;O ?V4H:V@=>W V=T:FVW V=AC;V=C 0=BCA® C ?0FVT=BV2 7 FC:@>28< 4V015B< V=AC;V=

3;0@3V= H284;> <5B01>;V7CTBLAO =0 :0@1>:A8;L=>@5==O< 42>E 0:B82=8E <5B01>;VBV2 M1 (21A-3;VF8=-V=AC;V=) V M2 (21A-3;VF8=-457-30B-B@5>=V=-V=AC;V=). # ?;072V 3>;>2=>N F8@:C;NNG>N A?>;C:>N T <5B01>;VB 1. :A?>78FVO 1 7@>AB0T ?@>?>@FV9=> 22545=V9 4>7V V=AC;V=C 0=BCA. \$0@<0>:V=5B8G=V B0 D0@<0>:48=0 B5, I> 5D5:B ?V4H:V@=>W V=T:FVW V=AC;V=C 0=BCA® ?>2O70=89 ?5@5206=> V7 5:A?>78FVTN 1. =AC;V= 3;0@3V= B0 <5B01>;VB 2 C 1V;LH>ABV CG0A=8:V2 4>A;V465=L =5 28O2;O;8AO, 0 :>;8 WE=V9 2®.

:;V=VG=8E 4>A;V465==OE ?@8 0=0;V7V ?V43@C?, AD>@<>20=8E 70 2V:× V AB0BBN, =5 1C;> 28O2;5=> @V7=8FV C ?>:07=8:0E 157?5G=>ABV B0 5D5:B82=>ABV

VB8 B0 ?V4;VB:8

\$0@<0>:V=5B8:0 ?@5?0@0BC C 4VB59 7 FC:@>28< 4V015B>< 1 B8?C 2V:× 2V4 2 4> <5=H =V6 6 @>:V2 >FV=N20;0AO C >4=>A;V465==V (482. @>74V; «\$0@<0>:48=0B@82V, 70 @57C;LB0B0<8 O:>3> 1C;> 2AB0=>2;5=>, I> 70:>=>ABV 7=F5=B@0FV9 2 ?;072V ?>4V1=V 4> B0:8E C 4>@>A;8E, V =5 1C;> 28O2;5=> 6>4=8E 4>:07V2 =0 :>@8ABL :C 9>3> <5B01>;VBV2 ?@8 B@820;>AC20==V ?@5?0@0BC. >::V=VG=V 40=V 7 157?5:8

>::V=VG=V 40=V, >B@8<0=V C @0A;V465=L 7 282G5==O D0@<0>;>3VG=>W 157?5:8, B>:A8G=>ABV ?@8 1030B>:@0B=>AC20==V ?@5?0@0BC, 35=>B>:A8G=>ABV, :0=F5@>35==>3> ?>B5=FV0;C V B>:A8G=>ABV 4;O @5?@>4C:B82=>W DC=:FVW, =5 28O28;8 >A>1;82>W =5157?5:8 4;O ;N48=8.

\$0@<0F52B8G=V E0@0:B5@8AB8:8.

A=>2=V DV78:>-EVABV: 15710@2=89 01> <0965 15710@2=89 ?@>7>@89 @>7G8=.

5AC

&59 ;V:0@AL:89 70AV1 =5<>6=0 7 H?@8F8 =5 3> V=H>3> <0B5@V0;C.

"5@ABV.

0@B@846V 3 @>:8.

\$;0:>=8 3 @>:8.

"5@ABV ?VA;O ?5@H>3> 28:>@8AB0==O :0@B@8460

&59 ;V:0@AL:89 70AV1 A;V4 715@V30B8 ?@>BO3× <0:A8 +30 °C C 70E8I5=>

VA;O :>6=>W V=T:FVW H?@8F-@CG:C A;V4 7=>2C 70:@820B8 :>2?0G:× 7 <5B>N 70E8ABC 2V4 A2VB;0.

"5@ABV ?VA;O 2V4:@8BBO D;0:>=C

15@V30B8 ?@>BO3>< <0:A8C 2 >@83V=0;L=V9 C?0:>2FV C 70E8I5==> C 7>2=VH=V9 :0@B>==V9 C?0:>2FV 7 <5B>N 70E8ABC 2V4 A2VB;0.

5:×<5=4CTBLAO 707=0G0B8 =0 5B8:5BFV 40BC ?5@H>3> 2V4:@8BBO D;0:>=0.

#<>28 715@V30==O.

15@V30B8 C =54>ABC?=8E 4;O 4VB59

52V4:@8BV :0@B@846V

15@V30B8 ?@8 B5+2 °C - +8 °C. 5 70<>@>6C20B8!

5 4>?CA:0B8 :>=B0:BC 7 <>@>78;L=8< 2V44V;5==O< 01> =0:>?8GC20G0<8 E>;>4C.

15@V30B8 :0@B@846 C 7>2=VH=V9 :0@B>==V9 C?0:>2FV 7 <5B>N 70E8ABC 2V4 A2VB;0.

0@B@846V ?VA;O ?5@H>3> 28:>@8AB0==O

#<>28 715@V30==O 482VBLAO C @>74V;V «"5@ABV».

52V4:@8BV D;0:>=8

15@V30B8 ?@8 B5+2 °C - +8 °C. 5 70<>@>6C20B8!

5 4>?CA:0B8 :>=B0:BC 7 <>@>78;L=8< 2V44V;5==O< 01> =0:>?8GC20G0<8 E>;>4C.

15@V30B8 D;0:>= C 7>2=VH=V9 :0@B>==V9 C?0:>2FV 7 <5B>N 70E8ABC 2V4 4VW A2VB;0.

\$;0:>=8 ?VA;O 2V4:@8BBO

#<>28 715@V30==O 482VBLAO C @>74V;V «"5@ABV».

#?0:>2:0.

5: ?> 3 <; C :0@B@846V; ?> 5 :0@B@846V2 C 1;VAB5@V; ?> 1 1;VAB5@C 2 :0@B>==V9 :>@>1FV;

1: ?> 10 <; C D;0:>=V; ?> 1 D;0:>=C 2 :0@B>==V9 :>@>1FV.

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

8@>1=8:.

«!0=>DV-25=BVA >9G;0=4<1%», V<5GG8=0/
Sanofi-Aventis Deutschland GmbH, Germany.

VAF57=0E>465==O.

@N=V=3HB@0AA5 50 600, H500, H590 65926 \$@0=:DC@B-=0-09=V, V<5GG8=0/
Bruningstrasse 50 600, H500, H590 65926 Frankfurt am Main, Germany.

;0A=8: B>@3>2>W ;VF5=7VW.

"«!0=>DV-25=BVA #:@0W=0», #:@0W=0.