

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

5-\$"# &
(5-FLUOROURACIL EBEWE)

!;:04:

4VNG0 @5G>28=0: DB>@C@0F8; (fluorouracil);
1 <; :=F5=B@0BC
4>?>28=8: =0B@VN 3V4@>:A84, 2>40 4;O V=T:FV9.

V:0@AL:0 D>@<0. :=F5=B@0B 4;O @>7G8=C 4;O V=DC7V9.

\$0@<0:>B5@0?52B8G=0 3@C?0. =B8=5>?:0AB8G=V 70A>18. =B8<5B01>;VB8. !B@C:BC@=V 0=0;>38
?V@84 "L01B C02.

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

>:070==O.

V:C20==O @0:C <>;>G=>W 70;>78 V :>;>@5:B0;L=>3> @0:C (C 283;04V <=>=>B5@0?VW 01> 2 :>
<1V=0FVW 7 V=H8<8 0=B8=5>?:0AB8G=8<8 70A>10<8).

V:C20==O @0:C H;C=:0, @0:C 3>;>28 B0 H8W V @0:C ?V4H;C=:>2>W 70;>78.

@>B8?>:070==O.

- V?5@GCB;82VABL 4> DB>@C@0F8;C01> 4> 1C4L-O:>3> 7 :=5=BV2 ?@5?0@0BC.
 - @83=VG5==O DC=:FVW :VAB:>2>3><>7:C, >A>1;82> ?VA;O ?@>5=52>W B5@0?VW 01>
- ;V:C20==O V=H8<8 ?@>B8?CE;8==8<8 ?@5?0@0B0<8.
- VT;>AC?@5AVO.
 - =0G=V 2V4E8;5==O :V;L:>ABV D>@<5=8E 5;5<5=BV2 C :@>2V.
 - @>2>B5GV.
 - !B><0B8B8, 28@07:8 A;87>2>W >1>;>=:8 @>B0 V H;C=:> 2>-.8H:>2>3> B@0:BC.
 - "06:0 4V0@50.
 - "06:V ?>@CH5==O DC=:FVW ?5GV=:8 B0/01> =8@>:.
 - "06:V V=D5:FV9=V 70E2>@N20==O (=0?@8;:04 >?5@V7CNG89 ;8H09, 2VB@O=0 2VA?0).
 - !8;L=5 28A=065==O (:0E5:AVO).
 - V25=L 1V;V@C1V=C 2 ?;072V > 85
 - # ?5@V>4 ;V:C20==O DB>@C@0F8;< =5>1EV4=> C=8:0B8 20:F8=0FVW 6828<8 20:F8=0<8.
 - 5@V>4 203VB=>ABV 01> 3>4C20==O 3@C44N.

\$B>@C@0F8; =5 <>6=0 70AB>A>2C20B8 >4=>G0A=> 7 1@82C48=><, A>@82C48=>< 01> 7 WE=V<8
0=0;>30<8. @82C48=, A>@82C48= B0 0=0;>38 ?>BC6=V V=3V1VB>@8 D5@<5=BC 483V4@>?V@8
35=078 (), I> @C9=CT DB>@C@0F8;.

@8

0FVT=B0< 7 45DVF8B>< D5@<5=BC =5 A;V4 ?@87=0G0B8 DB>@C@0F8;.

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

>78 V AE5<0 B5@0?VW 287=0G0NBLAO V=482V4C0;L=> 70;56=> 2V4 AB0=C ?0FVT=B0 V 284C @0:C,
0 B0:>6 70;56=> 2V4 B>3>, 70AB>A>2CTBLAO 5-DB>@C@0F8; 1525C 283;04V <=>=>B5@0?VW 01> C
:><1V=0FVW 7 V=H8<8 2840<8 ;V:C20==O. ">G=5 4>7C20==O =5>1EV4=> 4V7=020B8AO 7

B5@0?52B8G=8E ?@>B>:;>V2, O:V 28O28;8AO 5D5:B82=8<8 2 ;V:C20==V ?52=>W E2>@>18.

>G8=0B8 ;V:C20==O 5-DB>@C@0F8; 1525=5>1EV4=> 2 C<>20E AB0FV=>0@C. 030;L=0 4>1>20 4>70
4;O 4>@>A;8E =5 ?>28==0 ?5@528IC20B8 1 3.

0728G09 4>@>A;8< 4>78 287=0G0NBL 7 @>7@0EC=:C =0 1 :3 @50;L=>W <0A8 BV;0 ?0FVT=B0, >4=0:

E2>@8< 7 =04N <0A>N BV;0, =01@O:0<8, 0AF8B>< B0 V=H8<8 D>@<0<8 ?0B>;>3VG=>W 70B@8

@30=V778 287=0G0NBL 7 @>7@0EC=:C =0 1 :3 V450;L=>W <0A8 BV;0.

5-DB>@C@0F8; 152522>4OBL H;OE<< 2=CB@VH=L>25==8E V=T:FV9, 2=CB@VH=L>25==8E
V=DC7V9 01> 2=CB@VH=L>0@B5@V0;L=8E V=DC7V9.

86G5 =02545=V >@VT=B>2=V @5:><5=40FVW I>4> 4>7.

V:C20==O :>:>@5:B0;L=>3> @0:C

V4 G0A ?>G0B:>2>3> :C@AC B5@0?VW ?@5?0@0B <>6=0 22>48B8 H;OE<< V=DC7V9 01> V=T:FV9.
=DC7VW :@0I5, >A:V;L:8 ?@8 B0:>A>1V 22545==O 28=8:0T <5=H5 B>:A8G=8E 5D5:BV2.

=CB@VH=L>25==V V=DC7VW. >1>2C 4>7C 15 <3/:3 <0A8 BV;0 (600 <3/<2 ?>25@E=V BV;0), 0;5 =5
1V;LH5 1 3/V=DC7VN, @>72>4OBL 300-500<; 5 % @>7G8=C 3;N:>78 01> 0,9 % @>7G8=C =0B@VN
E;>@84C. >7G8= 4;O V=DC7V9 22>4OBL 2=CB@VH=L>25==> ?@>BO3<< 4 3>48=. # =0ABC?=V 4=V
?@5?0@0B 22>4OBL C B0:V9 65 4>7V, 4>:8 =5 ?@>O2;ONBLAO B>:A8G=V 5D5:B8 01> 7030;L=0 4>70
=5 4>AO3=5 12-15 3. 5O:8< ?0FVT=B0< 22>48;8 4> 30 3 DB>@C@0F8;C ?> 1 3 =0 4>1C (<0:A8<0;L=0
4>1>20 4>70). @8 ?>O2V =51060=8E ?>1VG=8E 5D5:BV2 7 1>:C A8AB5<8 :@>2>B2>@5==O 01>
H;C=:>2>-.8H:>2>3> B@0:BC =0ABC?=5 22545==O ?@5?0@0BC 2V4.;040NBL 4> 2V4=>2;5==O 35
<0B>;>3VG=8E ?>:07=8:V2 V 7=8:=5==O B>:A8G=8E 5D5:BV2. ;LB5@=0B82=> 5-DB>@C@0F8; 1525
<>6=0 22>48B8 H;OE<< 157?5@5@2=8E 24-3>48==8E 2=CB@VH=L>25==8E V=DC7V9.

=CB@VH=L>25==V V=T:FVW. > 12 <3/:3 <0A8 BV;0 (480 <3/<2 ?>25@E=V BV;0) 22>4OBL H;OE<<
2=CB@VH=L>25==8E V=T:FV9 I>4=O ?@>BO3<< 3 4=V2. @8 2V4ACB=>ABV >7=0: B>:A8G=8E
5D5:BV2 <>6=0 ?@>4>26C20B8 22>48B8 ?@5?0@0B C 4>7V 6 <3/:3 <0A8 BV;0 (240 <3/<2 ?>25@E=V
BV;0) C ?OB89, AL<<89 V 452OB89 4=V :C@AC. ;O ?V4B@8W B5@0?VW ?@5?0@0B 22>4OBL C 4>7V
5-10 <3/:3 <0A8 BV;0 (200-400 <3/<2 ?>25@E=V BV;0) 1 @07 =0 B8645=L.

@8 ?>O2V =51060=8E ?>1VG=8E 5D5:BV2 =0ABC?=5 22545==O ?@5?0@0BC 2V4.;040NBL 4>
7=865==O B>:A8G=8E 5D5:BV2.

V:C20==O @0:C <>:>G=>W 70;>78

;O ;V:C20==O @0:C <>:>G=>W 70;>78 5-DB>@C@0F8; 152570AB>A>2CNBL C :<<1V=0FVW 7 V=H8<8
EV?@5?0@0B0<8, =0?@8.;04 <5B>B@5:A0B<< V F8.;>D>AD0< 01> 4>:A>@C1VF8=<< V F8.;>D>AD0
@8 B0:8E AE5<0E ;V:C20==O 5-DB>@C@0F8; 152522>4OBL 2=CB@VH=L>25==> ?>

10-15 <3/:3 <0A8 BV;0 (400-600 <3/<2 ?>25@E=V BV;0) C ?5@H89 V 2>AL<89 4=V :C@AC B@820;VABN
28 4V1.

5-DB>@C@0F8; 1525B0:>6 <>6=0 22>48B8 H;OE<< 157?5@5@2=8E 24-3>48==8E 2=CB@VH=L>25==8E
V=DC7V9, ?@8 FL>70 AB0=>28BL 8,25 <3/:3 <0A8 BV;0

(350 <3/<2 ?>25@E=V BV;0).

=HV A?>A>18 22545==O

=CB@VH=L>0@B5@V0;L=V V=DC7VW. >1>2C 4>7C 5-7,5 <3/:3 <0A8 BV;0 (200-300 <3/<2 ?>25@E=V
BV;0) 22>4OBL H;OE<< 157?5@5@2=>W 24-3>48==>W 2=CB@VH=L>0@B5@V0;L=V V=DC7VW. #
45O:8E 28?04:0E <>6CBL 70AB>A>2C20B8AO @53V>=0;L=V 2=CB@VH=L>0@B5@V0;L=V V=DC7VW
4;O ;V:C20==O ?5@28==8E ?CE;8= 01> <5B0AB07V2.

A>1;82V 3@C?8 ?0FVT=BV2

=865==O 4>7 @5:><5=4CTBLAO C @07V :0E5:AVW, A5@9>7=8E EV@C@3VG=8E 2B@CG0=L C
?>?5@54=V 30 4=V2, ?@83=VG5==O DC=:FVW :VAB:>2>3><>7:C, 0 B0:>6 ?@8 =0O2=>ABV
?>@CH5=L DC=:FVW ?5GV=:8 01> =8@>:.

@8 ;V:C20==V ;VB=VE E2>@8E :>@83C20B8 4>78 =5<0T ?>B@518.

018@0B8 @>7G8= 7 D;0:>=0/01EV4=> 157?>A5@54=L> ?5@54 28:>@8AB0==O

/:I> 2 @57C;LB0BV >E>;>465==O 2 ?@5?0@0BV CB2>@8BLAO >A04, 9>3> @>7G8=ONBL H;OE<<
=03@V20==O 4> 60 !B0 V=B5=A82=>3> 71>2BC20==O. 5@54 70AB>AC20==O< ?@5?0@0B

>E>;>46CNBL 4> B5

>1VG=V @50:FVW.

0;V =02545=V :0B53>@VW G0AB>B8 =51060=8E @50:FV9:

C65 G0AB>: ≥1/10; G0AB> >1/100, <1/10; =5G0AB> ≥ 1/1000, < 1/100; @V4:> ≥ 1/10 000, <1/1 000;
?>>48=>:V <1/10 000; '0AB>B0 =52V4<<0 (=5 <>65 1CB8 2AB0=>2;5=0 =0 >A=>2V =0O2=8E 40=8E).

=D5:FVW B0 V=207VW

5G0AB>. @>?0A=8FO.

'0AB>B0 =52V4<<0. =D5:FV9=V 70E2>@N20==O, A5?A8A.

I>:C A8AB5<8 :@>2V B0 ;VW A8AB5<8

C65 G0AB>. VT;>AC?@5AVO (>48= 7 4>7>;VIVG=8E 5D5:BV2), =59B@>?5=VO B0 B@>
<1>F8B>?5=VO (>1842V 2V4 A5@54=L>3> 4> 2:@09 BO6:>3> ABC?5=O BO6:>ABV), ;59:>?5=VO,
03@0=C;>F8B>7, 0=5A>2V :@>2>B5GV B0 ?0=F8B>?5=VO.

!BC?V=L BO6:>ABV (ABC?5=V - IV 70 H:0;>N 0FV>=0;L=>3> V=AB8BCBC @0:C !(, NCI) AC?@5AVW
70;568BL 2V4 <5B>4C 22545==O ?@5?0@0BC (2=CB@VH=L>25==>, 1>;NA>< G8 2=CB@VH=L>25==>
157?5@5@2=0 V=DC7VO) B0 2V4 9>3> 4>7C20==O. 59B@>?5=VO @>72820TBLAO ?VA;O :>6=>3>
B5@0?52B8G=>3> F8;;C 7 2=CB@VH=L>25==>8< 1>;NA=8< 22545==O< DB>@C@0F8;C C 2V4?>2V4=8E
4>70E (<0:A8<0;L=5 7=865==O ?>:07=8:V2 =59B@>DV;V2: =0 9 14-9 (- 20-9) 45=L ;V:C20==O;
?>25@=5==O 4> =>@<0;L=8E 7=0G5=L: 70728G09 ?VA;O 30-3> 4=O).

I>:C VW A8AB5<8

C65 G0AB>. AC?@5AVO 7V 71V;LH5==O< G0AB>B8 V=D5:FV9.

V4:>. >6CBL 2V41C20B8AO 35=5@0;V7>20=V 0;5@3VG=V @50:FVW, 2;;NG=> 7 0=0DV;0:B8G=8< H>:>
5B0I>;VG=V @>7:048

>>48=>:V. 878: @>728B:C BO6:8E V B@820;8E ?>1VG=8E @50:FV9 =524>27V ?VA;O ?>G0B:C
;V:C20==O DB>@C@0F8;< =0928I89 C ?0FVT=BV2 7 =87L:8<8 @V2=O<8 0:B82=>ABV 483V4@>?V@8
35=078 () (7 1C4L-O:>W ?@8G8=8, 7>:@5<0 2=0A;V4>: ?@89>@V2 B8?C 5=V;C@0F8;C 01>
?>B82V@CA=>3> ?@5?0@0BC A>@82C48=C).

5:><5=4CTBLAO :>=B@>;N20B8 0:B82=VABL =0 ?>G0B:C ;V:C20==O.

I>:C =5@2>2> W A8AB5<8

5G0AB>. >6;8289 B@0=78B>@=89 >1>@>B=89 F5@51@0;L=89 A8=4@<, ?@8 O:>AB5@V30NBLAO
0B0:AVO, A?;CB0=VABL A2V4>>ABV V 5:AB@0?V@02V V :>@B8:>A?V=0;L=V @>7;048, =VAB03<,
3>;>2=89 1V;L, 70?0<>@>G5==O, 59D>@VO.

5G0AB>. !>;82VABL, 457>@VT=B0FVO, 3>AB@89 <>7>G:>289 A8=4@>

>>48=>:V. >2V4><;O;>AO ?@> A8<8 ;59:>5=F5D0;>?0BVW: 2B@0B0 ?0<OBV, ?0@5AB57VO,
;5B0@3VO, A;01:VABL<07V2, ?>@CH5==O <>28, :><0, AC4<<8. 878: @>728B:C ;59:>5=F5D0;>?0BVW
28I89 C ?0FVT=BV2 7 45DVFB8>< 483V4@>?V@835=078. ;O 4V03=>AB8:8 ;59:>5=F5D0;>?0BVW
4>FV;L=> 70AB>A>2C20B8 <5B>4 48DC7V9=> 72065=>W B><>3@0DVW. @8 :><1V=>20=V9 EV
B5@0?VW (7>:@5<0 DB>@C@0F8;>< C ?>T4=0==V 7 <! 01> F8A?;0B8=><) 2V4;>2=>3> <>7:C.

DB0;L<>;>3VG=V @>7:048

5G0AB>. 047>B5G0, =5GVB:VABL 7>@C, ?>@CH5==O <>B>@8:8 >:0, =52@8B 7>@>2>3> =5@20,
48?;>?VO, 7=865==O 3>AB@>B8 7>@C, A2VB;>1>O7=L, :>='N=:B82VB, 1;5D0@8B, @C1F5289
5:B@>?V=>, DV1@>7 A;V7=8E :0=0;LHV2.

I>:C A5@F52>W A8AB5<8

C65 G0AB>. >@CH5==O , E0@0:B5@=V 4;O VH5

'0AB>. V;L 2 3@C4=V9 ;;VBFV, O:89 AE>689 =0 AB5=>:0@4VN.

5G0AB>. @8B:0@40, VH5:0@40, :0@48B, A5@F520 =54>AB0B=VABL, 48;OB0B82=0 :0@4V>?0BVO B0
:0@4V>35==89 H>:.

>>48=>:V. C?8=:0 A5@FO B0 @0?B>20 A5@F520 A<5@BL.

0@4V>B>:A8G=V ?>1VG=V 5D5:B8 ?5@5206=> @>72820NBLAO ?V4 G0A 01> ?@>BO3< 45:V;L:>E
3>48= ?VA;O ?5@H>3> B5@0?52B8G=>3> F8;;C.

0FVT=B8 7 265 VA=CNG>N VH5N E2>@>1>N A5@FO 01> :0@4V>?0BVTN <0NBL 1V;LH89 @878:
@>728B:C :0@4V>B>:A8G=8E ?>1VG=8E 5D5:BV2.

!C48==V @>7:048

5G0AB>. >A>2V :@>2>B5GV, 0@B5@V0;L=0 3V?>B5=7VO, B@><1>D;51VB, A8=4@< 59=>, B@><1>5
<1>;VW, @>7H8@5==O 25=, ?5@8D5@8G=0 =59@>?0BVO, 20A:C;VB.

I>:C 48E0;L=>W A8AB5<8

C65 G0AB>. □@>=E>A?07

I>:C H:C=:>2>:-:8H:>2>3> B@0:BC

C65 G0AB>. 0?0;5==O A;87>28E >1>;>=: (7>:@5<0 AB<0B8B, 57>D03VB, D0@8=3VB, ?@>:B8B).
V0@5O, =C4>B0, 1;N20==O. =>@5:AVO.

5G0AB>. 8@07:8 H;C=:>2>:-:8H:>2>3> B@0:BC, H;C=:>2>:-:8H:>2V :@>2>B5GV, 7=52>4=5==O, A5?A8A,
0 B0:>6 CB2>@5==O 28@07>: B0 H;C=:>2>:-:8H:>2V :@>2>B5GV, 2V4B>@3=5==O =5:@>B8G=8E<0A.

!BC?V=L BO6:>ABV (ABC?5=V IV 70 H:0;>N 0FV=>0;L=>3> V=AB8BCBC @0:C !, (NCI) ?>1VG=8E
5D5:BV2 7 1>:C H;C=:>2>:-:8H:>2>3> B@0:BC 70;568BL 2V4 <5B>4C 22545==O ?@5?0@0BC B0 2V4
9>3> 4>7C20==O. @8 281>@V 157?5@5@2=>W V=DC7VW O:<5B>4C 22545==O DB>@C@0F8;C, AB>
<0B8B G0ABVH5 AB0T ?@8G8=>N >1<565==O 4>78, =V6 AC?@5AVO.

5?0B>1V;V0@=V @>7:048

5G0AB>. 5GV=:>289 F8B>;VB8G=89 A8=4@>

C65 @V4>.: 5:@>78 ?5GV=:8 (G0A<< ;5B0;L=V), E>;5F8AB8B.

I>:C H:V@8 V?V4H:V@=8E B:0=8=

'0AB>. ;>?5FVO (>1>@>B=0).

5G0AB>. □5@<0B8B, 7:@5<0 ACEVABL H:V@8, B@VI8=8, 5@>7VW, 5@8B5<0, 28A8?0==O, A25@1V6,
D>B>GCB;82VABL, H:V@=V 0;5@3VG=V @50:FVW, ?V3<5=B0FVO, 3V?5@?V3<5=B0FVO 01> 45?V3
<5=B0FVO C 283;04V A1;87C 25=, 7:8E 4>7 V ?@8 B@820;8E 157?5@5@2=8E V=DC7VOE
DB>@C@0F8;C T A8=4@<< 4>;>=>-?V4>H>2=>W 5@8B@>4875AB57VW.

I>:C :VAB:>2>-<07>2>W A8AB5<8 V A?>;CG=>W B:0=8=8

5G0AB>. 5:@>7 =>A>28E :VAB>;<07>20 A;01:VABL.

I>:C =8@>: V A5G>284V;L=>W A8AB5<8

5G0AB>. 8@:>20 =54>AB0B=VABL, 3V?5@C@8:5

I>:C 5=4>:@8==>W A8AB5<8

5G0AB>. V428I5==O @V2=O 7030;L=>3> B8@>:A8=C (T4) V 7030;L=>3> B@89>4B8@>=V=C (T3) 2
A8@>20BFV 157 ?V428I5==O 2V;L=>3> T4 V B8@5>B@>?V=C 157 ;;V=VG=8E >7=0: 3V?5@B8@5>7C.

I>:C @5?@>4C:B82=>W A8AB5<8

5G0AB>. >@CH5==O A?5@<0B>35=57C V >2C;OFVW.

D5:B8 7030;L=>3> E0@0:B5@C V

5G0AB>. #B><0, 28A=065==O, 7030;L=0 0AB5=VO.

01>@0B>@=V ?>:07=8:8

>>48=>:V. □V4>48=>:V 28?04:8 71V;LH5==O ?@>B@<1V=>2>3> G0AC ?@8 :<1V=>20=>AC20==V
DB>@C@0F8;C V 20@D0@8=C.

5@54>7C20==O.

!8<8

>AB@V: ?A8E>B8G=V @50:FVW, A>;82VABL, ?>A8;5==O 4VW A540B82=8E ?@5?0@0BV2,

?>A8;5==O B>:A8G=>W 4VW 0;:>3>;N.

/:I> ?>B@V1=89 A540B82=89 5D5:B, <>6=0 ?@87=0G8B8 4V075?0< 2=CB@VH=L>25==> C <0;8E 4>70E
(=0?@8;:04 ?>G8=0NG8 7 5 <3) ?@8 ?>ABV9=>

%@>=VG=V: ?@83=VG5==O DC=:FVW :VAB:>2>3><>7:C, 06 4> @>728B:C 03@0=C;>F8B>7C V

:@8B8G=>W B@<1>F8B>?5=VW, B5=45=FVO 4> :@>2>B5G, 28@07:8 H;C=:>2>:-:8H:>2>3> B@0:BC,
4V0@50, 0;>?5FVO.

7=0:8 V=B>:A8:0FVW: =0ABC?=V ?>1VG=V @50:FVW ?@>02;ONBLAO ?> AB0==O ?5@54>7C20==O:

- =C4>B0;

- 1;N20==O;

- 4V0@50;

- BO6:5 70?0;5==O A;87>28E >1>;>=>;

- CB2>@5==O 28@07>: H;C=:>2>:-:8H:>2>3> B@0:BC B0 H;C=:>2>:-:8H:>2V :@>2>B5GV;

- AC?@5AVO (B@<1>F8B>?5=VO, ;59:>?5=VO, 03@0=C;>F8B>7).

V:C20==O

!75F8DVG=89 0=B84>B DB>@C@0F8;C =52V4<<89. ?@>DV;0:B8G=>N <5B>N <>6CBL/?>28==V

70AB>A>2C20B8AO B@0=ADC7VW ;59:>F8B0@=>3> 01> B@<1>F8B0@=>3> :>=F5=B@0BV2.

5>1EV4=> 70157?5GC20B8 045:20B=C 3V4@0B0FVN V 4VC@57, 0 B0:>6 :>@83C20B8 ?>@CH5==O

10;0=AC 5;5:B@>;V BV2. # 35<>4V0;V7V 70728G09 =5<0T ?>B@518. 0FVT=B ?>28=5= ?5@51C20B8 ?V4

?8;L=8< <548G=8< =03;04<< 4;0 O:><>30 1V;LH @0==L>3> 28O2;5==O 35<0B>;>3VG=8E V ?V7=VE

H;C=:>2>:-:8H:>28E CA;:04=5=L. >40;LH5 ;V:C20==O A8<0B8G=5.

@07V ?>028 >7=0: V=B>:A8:0FVW 22545==O DB>@C@0F8;C A;V4 =5309=> ?@8?8=8B8. !;V4

@>7?>G0B8 A8<0B8G=V B5@0?52B8G=V 70E>48.

8@065=C AC?@5AVN A;V4 ;V:C20B8 2 C<>20E AB0FV>=0@C. "5@0?VO AC?@5AVW 2;;NG0T, O:I>=5>1EV4=>, 2V4=>2;5==O 2B@0G5=8E :>=5=BV2 :@>2V B0 0=B810:B5@V0;L=C B5@0?VN. >65 7=04>18B8AO @>7
>=VB>@8=3 35<0B>;>3VG=8E ?>:07=8:V2 A;V4 ?@>2>48B8 ?@>BO3< 4 B86=V2 ?VA;O B>3>, O: 2V41C;>AO ?5@54>7C20==O.

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

03VB=VABL. 5-DB>@C@0F8; 1525=5 <>6=0 70AB>A>2C20B8 ?V4 G0A 203VB=>ABV. V=:8 @5?@>4C:B82=>3> 2V:C ?>28==V 70AB>A>2C20B8 5D5:B82=V :>=B@0F5?B82=V 70E>48. /:I> 203VB=VABL =0AB0T ?V4 G0A ;V:C20==O, @5:>5=4CTBLAO >B@8<0B8 :>=AC;LB0FVN 35=5B8:0. >4C20==O 3@C44N. @5?0@0B =5 <>6=0 70AB>A>2C20B8 ?V4 G0A 3>4C20==O 3@C44N. \$5@B8;L=VABL. \$B>@C@0F8; <>65 A?@02;OB8 =530B82=89 2?;82 =0 @5?@>4C:B82=C A8AB5;>2V:0<, O:V >45@6CNBL B5@0?VN DB>@C@0F8;<, =5 @5:><5=4CTBLAO 70G8=0B8 48B8=C ?V4 G0A ;V:C20==O, 0 B0:>6 ?@>BO3< 6 ;>2V:0< A;V4 ?@>048B8 ?5@54 ?>G0B:< ;V:C20==O ?@>:>=AC;LBC20B8AO 7 D0EV2FO<8 7 ?@>82>4C :@V>:>=A5@20FVW A?5@<8, >A:V;L:8 70AB>AC20==O DB>@C@0F8;C <>65 ?@>8725AB8 4> =572>@>B=>3> 157?;V44O.

VB8

5:<>5=40FVW I>4> ;V:C20==O DB>@C@0F8;< 4VB59 =5 @>7@>1;5=V.

A>1;82V 70E>48 157?5:8.

/: V ?@8 @>1>BV 7 V=H8<8 F8B>B>:A8G=8<8 ?@5?0@0B0<8, ?@8 <0=V?C;OFVOE 7 5-DB>@C@0F8;> < 1525=5>1EV4=> 4>45@6C20B8AO ?@028; 157?5:8. :>@8ABC20B8AO 70E8A=8< >4O3<< (E0;0B0<8, H0?>G:0<8, <0A:0<8, >:C;O@0<8 V >4=>@07>28<8 @C:028G:0<8), ?@8 <>6;82>ABV ?@0FN20B8 2 A?5FV0;L=> 2V42545=> 5>1EV4=> C=8:0B8 ?>B@0?;O==O @>7G8=V2 DB>@C@0F8;C =0 H:V@C V A;87>2V >1>;>=:8. /:I> 6 F5 B@0?8;>AL, WE @5B5;L=> ?@><820NBL 2>4>N 7 <8;>B@0?;O==V @>7G8=V2 DB>@C@0F8;C 2 >GV WE =5>1EV4=> ?@><8B8 25;8:>N :V;L:VABN 2>48 V =5309=> 725@=CB8AO 70<548G=>N 4>?><3>N. 03VB=V <548G=V ?@0FV2=8:8 =5 ?>28==V ?@0FN20B8 7 ?@5?0@0B>

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

V:C20==O 5-DB>@C@0F8;< 1525?>28==> 74V9A=N20B8AO ?V4 =03;O4<< :20;VDV:>20=>3> ;V:0@O->=>:>30, I> <0T 4>A2V4 70AB>AC20==O ?>BC6=8E 0=B8<5B01>;VBV2. >G8=0B8 ;V:C20==O DB>@C@0F8;<< =5>1EV4=> 2 C<>20E AB0FV>=0@C. >H:>465==O ABV=>. :8H:V2=8:0 ?@8 B5@0?VW DB>@C@0F8;< ?>B@51CT A8<0B8G=>3> ;V:C20==O 70;56=> 2V4 ABC?5=O BO6:>ABV, =0?@8;;04, 2V4=>2;5==O 2B@0B8 @V48=8. V0@5O ;53:>3> ABC?5=O <>65 :>=B@>;N20B8AO ?@>B84V0@59=8<8 ;V:0@AL:8<8 70A>10<8. 4=0: FL>3> =54>AB0B=L> 4;O ;V:C20==O 4V0@5W A5@54=L>3> ABC?5=O BO6:>ABV B0 BO6:>W 4V0@5W. 5@54 ?@87=0G5==O< B5@0?VW DB>@C@0F8;<< B0 ?V4 G0A =5W =5>1EV4=> ?@>2>48B8 =0ABC?=V ;V=VG=V >1AB565==O:
- I>45==89 >3;O4 @>B>2>W ?>@>6=8=8 B0 3;>B:8 4;O 28O2;5==O <>6;828E >7=0: C@065==O A;87>2>W >1>;>=:8;
- 7030;L=89 0=0;V7 :@>2V, 2;;NG=> 7 ?V4@0EC=< D>@<5=8E 5;5<5=BV2 :@>2V B0 B@> <1>F8BV2 ?5@54 :>6=8< 22545==O< DB>@C@0F8;C;
- 0=0;V7 1V>EV:07=8:V2 2>4=>-A>;L>2>3> >1
- ?5GV=>2V ?@>18.
@8 >4=>G0A=>AC20==V DB>@C@0F8;C B0 ?5@>@0;L=8E 0=B8:>03C;O=BV2 =5>1EV4=> ?@>2>48B8 @5B5;L=89 <>=VB>@8=3 ?@>B@><1V=>2>3> V=45:AC (?@>B@><1V=?> 2V:C). 5 <>6=0 ?@>2>48B8 20:F8=0FVN 6828<8 20:F8=0<8 ?V4 G0A B5@0?VW DB>@C@0F8;>4 ;V:C20==O DB>@C@0F8;<< A;V4 C=8:0B8 1C4L-O:8E :>=B0:BV2 7 ;N4L<8, O:V >B@8<0;8 20:F8=0FVN 2V4 ?>;V> @8 045:20B=>@C@0F8;<< 70728G09 @>72820TBLAO ;59:>?5=VO. V=V<0;L=0 :V;L:VABL ;59:>F8BV2 70728G09 A?>AB5@V30TBLAO ?5@54 AL<8< V G>B8@=04FOB8< 4=O<8 ?5@H>3> :C@AC B5@0?VW, 0;5 V=>4V
5:<>5=4CTBLAO I>4=O :>=B@>;N20B8 :V;L:VABL B@><1>F8BV2 V ;59:>F8BV2 V ?@8?8=OB8 ;V:C20==O C @07V 7=865==O :V;L:>ABV B@><1>F8BV2 4> @V2=O < 100 x 109%; 0 ;59:>F8BV2 < 3 E 10

9/;. @8 7<5=H5==V :V;L:>ABV ;59:>F8BV2 =86G5 2 E 109/; ,>A>1;82> ?@8 =0O2=>ABV
3@0=C;>F8B>?5=VW, @5:>5=4CTBLAO 3>A?VB0;V7C20B8 ?0FVT=BV2 C ;V:0@=O=89 V7>;OB>@ V
26820B8 70E>4V2 4;O 70?>1V30==O @>728B:C A8AB5<=8E V=D5:FV9. V:C20==O B0:>6 =5>1EV4=>
?@8?8=OB8 ?@8 ?>O2V ?5@H8E >7=0: AB<0B8BC 01> 28@07>: @>B>2>W ?>@>6=8=8, BO6:>W
4V0@5W, 28@07>: H;C=:>2>:-:8H:>2>3> B@0:BC, :@>2>B5GV 7V H;C=:>2>:-:8H:>2>3> B@0:BC, 0
B0:>6 ?@8 :@>2>B5G0E V :@>2>28;820E 1C4L-O:>W ;>:0;V70FVW.
\$B>@C@0F8; <0T 2C7L:89 <:>@84>@ 157?5:8» - @V7=8FO 1EV4=> @5B5;L=> 2V418@0B8 ?0FVT=BV2
V ?V418@0B8 4>78. \$B>@C@0F8; =5>1EV4=> 7 >15@56=VABN ?@87=0G0B8 E2>@8< 7 ?>@CH5==O<
DC=:FVW =8@>: 01> ?5GV=:8, 0 B0:>6 6>2BO=8F5N. 15@56=VABL B0:>6 =5>1EV4=0 ?@8 ;V:C20==V
?0FVT=BV2, C O:8E 7 ?>?5@54=VE :C@AV2 B5@0?VW 28=8:02 1V;L C 3@C4OE, 0 B0:>6 E2>@8< 7
:0@4V>;>3VG=8<8 70E2>@N20==O<8 2 0=0<=57V. # @07V BO6:8E :0@4V>B>:A8G=8E 5D5:BV2
;V:C20==O DB>@C@0F8;< B@510 ?@8?8=8B8. \$B>@C@0F8; <65 G8=8B8 B>:A8G=C 4VN =0
A5@F52C A8AB5O28 70E2>@N20=L A5@4FO 2 0=0<=57V.
A>1;820 >15@56=VABL =5>1EV4=0 ?@8 ;V:C20==V ?0FVT=BV2 3@C?8 28A>:>3> @878:C (O:V
>45@60;8 28A>:V 4>78 ?@<5=52>W B5@0?VW =0 4V;O=:C B070, 0;:V;CNGV ?@5?0@0B8, 0 B0:>6
?0FVT=BV2, O:V ?5@5=5A;8 04@5=0;5:B> 3V?>DV75:B>
V4 G0A ;V:C20==O DB>@C@0F8;< V ?@>BO3< 3 ;>2V:8, V 6V=:8) ?>28==V :>@8ABC20B8AO
2V4?>2V4=8<8 :>=B@0F5?B82=8<8 70A>10<8.

**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.**

\$B>@C@0F8; <65 28;:8:0B8 =C4>BC V 1;N20==O, B0:8< G8=>< ?>@CHCNG8 740B=VABL :5@C20B8
B@0=A?>@B=8<8 70A>10<8 V <5E0=V7<0<8. 0FVT=B0< A;V4 CB@8<0B8AO 2V4 :5@C20==O 02B> B0
2V4 @>1>B8 7V A;:04=8<8 <5E0=V7<0<8, O:I> 2>=8 >B@8@C@0F8;>

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

<548G=V9 ;VB5@0BC@V >?8ACTBLAO :<1V=>20=0 B5@0?VO DB>@C@0F8;< C ?>T4=0==V 7
:0;LFDV D>;V=0B>< (D>;V=>2>N :8A;>B>N). @8 B0:V9 :<1V=>20=V9 B5@0?VW DB>@C@0F8; <65
A?@8G8=OB8 1V;LH BO6:V ?>1VG=V 5D5:B8, 7>:@5<0 BO6:C 4V0@5N.
D5:B82=VABL V B>:A8G=VABL B5@0?VW 71V;LHCTBLAO C @07V 70AB>AC20==O DB>@C@0F8;C
2 ?>T4=0==V 7 V=H8<8 F8B>B>:A8G=8<8 ?@5?0@0B0<8 (F8;:>D>AD0<, 2V=:@8AB8=><,
<5B>B@5:A0B><, F8A?;0B8=><, 4>:A>@C1VF8=><), V=D5@=>=> D>;V=>2>N :8A;>B>N. @8 :>
<1V=>20=V9 B5@0?VW C ?>T4=0==V 7 V=H8<8 ?@5?0@0B0<8, I> ?@83=VGCNBL DC=:FVN
:VAB:>2>3> <>7:C, =5>1EV4=0 :>@5:FVO 4>7 DB>@C@0F8;C. =865==O 4>7 B0:>6 <>65 1CB8
>B@V1=> C @07V AC?CB=L>W 01> ?@<5=52>W B5@0?VW. \$B>@C@0F8; <65 ?>A8;N20B8
?@>O28 H:V@=8E ?@<5=528E C@065=L ?@8 ?@<5=52V9 B5@0?VW. 0@4V>B>:A8G=VABL
0=B@0F8;:V=V2 <>65 ?>A8;N20B8AO ?@8 :<1V=>20=>AC20==V 7 DB>@C@0F8;? >V4 G0A
;V:C20==O DB>@C@0F8;< =5 <>6=0 ?@89<0B8 0D5=07>=, D5=V;1CB07>= V AC;LD>=0?C@8=>;C
B>:A8G=VABL V 5D5:B82=VABL B5@0?VW DB>@C@0F8; <65 CBL 7=86C20B8AO.
%;>@4V075?>:A84, 48AC;LDV40<, 3@875>DC;L2V= B0 V7>=V0784 <>6CBL ?V428IC20B8
5D5:B82=VABL B5@0?VW DB>@C@0F8;>

\$B>@C@0F8; ?>A;01;NT 7030;L=V 70E8A=V <5E0=V7<8 >@30=V72V4L 7=86CTBLAO. 0AB>AC20==O
6828E 20:F8= C ?5@V>4 ;V:C20==O DB>@C@0F8;< <65 ?@8725AB8 4> ?>A8;5==O @5?;V:0FVW
2V@CAC.
>2V4><;O;>AO ?@> @>728B>: 35<>;V:-C@53> A8=4@>3> ;V:C20==O DB>@ C@0F8;< C ?>T4=0==V
7

&8<5B848= <>65 ?V428IC20B8 :>=F5=B@0FVN DB>@C@0F8;C 2 ?;072V.

5B@>=V407>; <>65 ?V428IC20B8 :>=F5=B@0FVN DB>@C@0F8;C 2 ?;072V V ?>A8;N20B8 B>:A8G=V
5D5:B8.

520; <>65 ?>A8;N20B8 35?0B>B>:A8G=VABL DB>@C@0F8;C.

"V07848 <>6CBL ?>A8;N20B8 B>:A8G=VABL ?@>B8?CE;8==8E ?@5?0@0BV2.

V=>@5;L1V= C ?>T4=0==V 7 DB>@C@0F8;< V D>;V=>2>N :8A;>B>N <>65 A?@8G8=OB8 A5@9>7=V
70?0;5==O A;87>28E >1>;>=>:.

5

\$5@<5=B 483V4@>?V@835=078 () 2V4V3@0T 206;82C @>;L C @>7?04V DB>@C@0F8;C. =0;>38

=C:;>784V2, B0:V O: 1@82C48= V A>@82C48=, <>6CBL ?@8725AB8 4> @V7:>3> ?V428I5==O 2 ?;07
=F5=B@0FVW DB>@C@0F8;C 01> V=H8E DB>@?V@8=09<5=H5 4-B86=52>3> V=B5@20;C <<
DB>@C@0F8;C B0 1@82C48=C, A>@82C48=C B0 WE 0=0;>3V2. # @07V =5>1EV4=>ABV
?@87=0G0TBLAO 4>A;V465==O 0:B82=>ABV D5@<5=BC 4> ?>G0B:C ?@>2545==O B5@0?VW V7
70AB>AC20==O< 5-DB>@?V@82>3> 70AB>AC20==O 1@82C48=C ?0FVT=B0<, O:V >B@8@C@0F8;>
<, =5>1EV4=> 268B8 5D5:B82=8E 70E>4V2, I>1 7<5=H8B8 B>:A8G=VABL DB>@C@0F8;C. 5:>
<5=4CTBLAO =5309=0 3>A?VB0;V70FVO. AV 70E>48 ?>28==V 1CB8 A?@G>20=V =0 70?>1V30==O
A8AB5<=8< V=D5:FVO< B0 453V4@0B0FVW.

@8 >4=>G0A=>W=C B0 DB>@C@0F8;C ?>2V4<;O;>AO ?@> ?V428I5==O 2 ?;07W=C, I> ?@872>48;>
4> ?>O28 A8:A8:0FVW D5=VB>W=>
6V=>:, O:V ?@89<0;8 4VC@5B8: BV0784=>3> B8?C 4>40B:>2> 4> F8:;>D>AD03VG=8E F8:;>V2
F8B>AB0B8:V2 157 BV0784C.

>2V4<;O;>AO ?@> :@5B@<<1V=C 70 2V:< C ?0FVT=BV2, O:V ?@89<0;8 20@D0@8= V 4>40B:>2>
>B@8@C@0F8; C 283;O4V <=>B5@0?VW 01> 2 :<1V=0FVW 7 ;520;>

?0FVT=B>: 7 @0:<< <>;>G=>W 70;>78, O:V >B@8<1V=0FVN 7 F8:;>D>AD0<, <5B>B@5:A0B<<,
DB>@C@0F8;>< V B0<:A8D5=><, A?>AB5@V302AO ?V428I5=89 @878: @>728B:C B@<<1>5
<1>;VG=8E O28I.

28?04:C >4=>G0A=>3> 70AB>AC20==O 2V=>@5;L1V=C B0 DB>@C@0F8;C/D>;V=>2>W :8A;>B8
<>65 @>72820B8AO 78B C BO6:V9 D>@ ?@872>48BL 4> ;5B0;L=>3> :V=FO.

030;L=V 2:07V2:8 4;O F8B>AB0B8:V2.

&8B>AB0B8:8 <>6CBL 7<5=HC20B8 CB2>@5==O 0=B8BV; ?VA;O 20:F8=0FVW ?@>B8 3@8?C.

&8B>AB0B8:8 <>6CBL 71V;LHC20B8 @878: V=D5:FVW ?VA;O 20:F8=0FVW 6828<8 20:F8=0<8.

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

\$0@<0:>48=0

\$B>@C@0F8; ?@>B8?CE;8==89 70AV1 7 3@C?8 0=B8<5B01>;VBV2. /: 0=B03>=VAB ?V@8
5-DB>@457>:A8C@848=.

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

IA>@1FVO

!>AB5@V30TBLAO 25;8:0 V=B5@- V V=B@020@V015;L=VABL ?>:07=8:V2 01A>@1FVW
DB>@C@0F8;C 7V H;C=:>2>.:8H:>2>3> B@0:BC ?VA;O ?5@>@0;L=>3> ?@89>@C@0F8; B0:>6
?V440TBLAO <5B01>;V73> ?@>E>465==O» C ?5GV=FV. V>4>ABC?=VABL DB>@C@0F8;C AB0=>28BL
0-80 %. >?CA:0TBLAO ;8H5 2=CB@VH=L>25==5 V 2=CB@VH=L>0@B5@V0;L=5 22545==O
DB>@C@0F8;C.

>7?>4V;

VA;O 2=CB@VH=L>25==>3> 22545==O DB>@C@0F8; @>7?>4V;OTBLAO 2 >@30=V7A>1;82> C
H284:> ?@>;VD5@CNG8E B:0=8=0E, B0:8E O: :VAB:>289<>7>:, A;87>20 >1>;>=:0 H;C=:>2>.:8H:>2>3>
B@0:BC V =>2>CB2>@5==O. \$B>@C@0F8; ?@>=8:0T G5@57 35<0B>5=F5D0;VG=89 V ?;0F5=B0@=89
10@T@8. 1T< @>7?>4V;C DB>@C@0F8;C AB0=>28BL 0,12 ;/:3<0A8 BV;0, 7207C20==O 7 1V;:0<8 ?;07
<8 :@>2V AB0=>28BL ?@81;87=> 10 %.

V>B@0=AD>@<0FVO

5B01>;V7< DB>@C@0F8;C 2V41C20TBLAO 2 ?5GV=FV V ?>4V1=89 4> <5B01>;V76 CB2>@NNBLAO
=5B>:A8G=V A?>;C:8 4V>:A84 2C3;5FN V A5G>28=0.

;V

!5@54=V9 ?5@V>4 =0?V2282545==O DB>@C@0F8;C 7 ?;07<8 :@>2V AB0=>28BL 10-20 E28;8= V
70;568BL 2V4 4>78. '5@57 3 3>48=8 ?VA;O 2=CB@VH=L>25==>3> 22545==O =57@C@0F8; C ?;072V =5
28O2;OTBLAO.

\$B>@C@0F8; 282>48BLAO ?5@5206=> G5@57 ;535=V C 283;O4V 4V>:A84C 2C3;5FN (60-80 %). "0:>6
DB>@C@0F8; 282>48BLAO =8@:0<8 C 283;O4V =57W 28EV4=>W A?>;C:8 (7-20 %), ?@81;87=> 170-180
<;/E2. # ?0FVT=BV2 7 ?>@CH5==O<8 DC=:FVW =8@>: DB>@C@0F8; 282>48BLAO ?>2V;L=VH5.

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

A=>2=V DV78:>-EVABV: ?@>7>@89 15710@2=89 01> A2VB;>-6>2B89 @>7G8=.

5AC

5-DB>@C@0F8; 1525=5>1EV4=> @>72>48B8 0,9 % @>7G8=>< =0B@VN E;>@84C 01> 5 % @>7G8=>< 3;N:>78.

5 1C;> 28O2;5=> =5ACABV 7 6>4=8< V7 28?@>1C20=8E @>7G8=V2-=>AVW2.

>2V4><;O:>AL ?@> =5AC

?0B8=, F8B0@01V=, 4V075?0<, 4>:A>@C1VF8=><, 4@>?5@84>;, DV;3@0AB8<, =VB@0B 30;VN, ;59:>2>@8=, <5B>B@5:A0B, <5B>::;>?@0

!C;V=0B>< 1525

!C;V=0BC 1525(100 <; 0;LFVC;V=0BC «1525» 10 <3/<;), 5000 <3 5-DB>@C@0F8;C 1525(100 <; 5-DB>@C@0F8;C 152550 <3/<;) V 40 <; 0,9 % @>7G8=C =0B@VN E;>@84C 2 V=DC7V9=>AV (?@8< B8?C Easy pump) T AB01V;L=>N ?@8 :V<=0B=V9 B5BO3>< 48 3>48=.

5-DB>@C@0F8; 1525=5 <>6=0 7

"5@ABV.

2 @>:8.

>7G8=8 4;O V=DC7V9 7 :>=F5=B@0FVTN 0,35 <3/<; V 15,0 <3/<;, ?@83>B>2;5=V H;OE<< @>72545==O 5-DB>@C@0F8;C 15255 % @>7G8=>< 3;N:>78 01> 0,9 % @>7G8=>< =0B@VN E;>@84C, T EV V DV78G=> AB01V;L=8< ?@>BO3>< 48 4V1 C @07V 715@V30==O ?@8 :V<=0B=V9 B5 2V4 A2VB;0 @8AB>2C9B5 BV;L:8 ?@>7>@V @>7G8=8.

>6;825 CB2>@5==O >A04C C 283;O4V :@8AB0;V2 C @07V 715@V30==O ?@8 B515 °C. 4=0: WE <>6=0 ?>2B>@=> @>7G8=8B8, ?V4V3@V20NG8 4> 60 °C =0 2>4O=V9 10=V, AC?@>2>46CNG8 V=B5=A82=8< 71>2BC20==O

#<>28 715@V30==O.

15@V30B8 2 >@83V=0;L=V9 C?0:>2FV ?@8 B5°C. 5 >E;>;>46C20B8 V =5 70<>@>6C20B8. 15@V30B8 C =54>ABC?=>

#?0:>2:0.

1 D;0:>= 7 15710@2=>3> A;0; 5 0==V9 :>@>1FV. \$;0:>= 7 :>@8G=52>3> A;0, 70:C?>@5=89 ?@>1:>N 7 1@><1CB8;>2>3> :0CGC:C V 0;N; 1 D;0:>= C :0@B>==V9 :>@>1FV.

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

0 @5F5?B>

8@>1=8:.

\$0@<0 5A.

EBEWE Pharma Ges.m.b.H. Nfg. KG.

VAF57=0E>465==O.

>=475THB@0A5,11,-4866 #=B5@0E, 2AB@VO.

Mondseestrasse,11, -4866 Unterach, Austria.